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HOWARD B. HUNT

President of the American Radium Society, 1952-1953

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SOME CURRENT TRENDS IN THERAPEUTIC RADIOLOGY*

By HOWARD B. HUNT, M.D.
OMAHA, NEBRASKA

MR. CHAIRMAN, Dean Moore, Members and Guests of the American Radium Society: We are all sincerely appreciative of the cordial greeting and reassuring welcome presented by Dr. Robert Moore, Dean of the Washington University School of Medicine. As you have learned, Washington University was founded in 1853 and we are now privileged to participate in its centennial celebration. At this time the American Radium Society pays homage to Washington University for its innumerable contributions of precious knowledge and inspiring leadership to the fields of medical science and practice. It was in the laboratories of this University that Professor Arthur Holly Compton conducted his basic research on the change in wavelength with scattering of radiation for which he was awarded the Nobel Prize in Physics in 1927 and the Gold Medal of the Radiological Society of North America in 1928. As further evidence of outstanding scientific contributions from this great university, the Nobel Prize in Medicine was awarded to Drs. Erlanger and Gasser in 1944 for their interpretation of the conduction of nerve impulses and to Drs. Carl and Gerty Cori in 1947 for their investigations of basic carbohydrate metabolism. Dr. Evarts A. Graham here initiated cholecystography for visualization and evaluation of the gallbladder in 1923, and pneumonectomy for cure of cancer of the lung in 1933. In its relation to the American Radium Society, Washington University School of Medicine has made the distinctive contribution of three of our thirty-three past presidents—Dr. Edwin C. Ernst, 1928, Dr. Sanford Withers, 1931 and Dr. Axel N. Arneson, 1947; also two first vice-presidents—Dr. LeRoy Sante and Dr. Wendell G. Scott.

At this point I shall digress from extolling a few of the grand contributions of Washington University in celebration of her centennial and turn to a general discussion of some of the current trends in medical teaching, research and practice, particularly as relating to the fields of cancer and therapeutic radiology. Diverse political, social, economic and scientific factors are at work: on the one hand, special medical services are being concen-

*President's Address delivered before the Thirty-fifth Annual Meeting, American Radium Society, St. Louis, Missouri, April 20–22, 1953.

trated more and more in large medical centers while, on the other, the usual conventional diagnostic and therapeutic services are being dispersed more and more to outlying communities.

During the past six years a stupendous national program has been developed in cancer research and practice through pooling of governmental and organizational funds which in 1952 alone amounted to over forty million dollars. Funds have been provided through the United States Public Health Service, the Atomic Energy Commission, the American Cancer Society, the Damon Runyon Fund and other state and voluntary agencies. Obviously, development of a service program in cancer would be impractical, allowing only about fifty dollars to each of the 770,000 cancer patients in the nation. Emphasis has been properly placed on teaching and research which by their nature funnel a significant proportion of the 40 million dollars into medical schools and their allied hospitals and institutions. Additional funds have been allocated primarily as construction grants (2 to 6 million dollars per year). Earlier diagnosis is being promoted through lay and professional education, cytologic examinations, mass roentgenologic surveys, general health surveys, tumor conferences and tumor clinics, thereby bringing more cases to surgery and radiotherapy at curable stages. Furthermore, revolutionary therapy is being developed in the form of chemotherapy, hormones, extraradical surgery and unique modalities in radiotherapy. These newer developments have been carried out and concentrated primarily in medical centers for the most part related to medical schools.

Current trends in radiotherapy are being significantly influenced by research and developments in the radioisotope division of the A.E.C. and in many university centers. Basic research in radiobiology is exemplified by our Janeway Lecture of today, "Some Factors Concerned in Recovery from Radiation Injury" by Dr. Leon O. Jacobson. A variety of new tools for research and radiotherapy have been elaborated in the nuclear reactors of the Atomic Energy Commission, and others are in the process of development. The clinical utilization of iodine-131 in the evaluation and treatment of thyroid disease and of phosphorus-32 in the treatment of leukemia and polycythemia is now well accepted. At this scientific session further contributions will be made on the use of radiogold and radioactive chromic phosphate in intracavitary carcinomatosis and on the interstitial use of radiogold in carcinoma of the prostate and in carcinoma of the cervix uteri, as well as on the use of radiostrontium in diseases of the eye. Dosimetric studies on the intracavitary and interstitial use of radiocobalt will be reviewed preparatory to its widening application in lieu of radium. The Oak Ridge Institute of Nuclear Studies is actively cooperating with some twenty-eight medical schools in the development of a telecurie therapy program utilizing radiocobalt, cesium or europium which may prove to be economic sources of radiation of from 600 to 2,000 kilovolt equivalent. Dr. Lee Farr of Brookhaven Laboratories reports here on the treatment of brain tumors through thermal neutron capture by boron, a worthwhile investigation but not a particularly promising departure from conventional therapy.

In the development of this national program, many university medical centers have enjoyed special privileges of access to Atomic Energy Commission products and special consideration in the allotment of both federal and private funds as a result of their extensive participation in the cancer research and teaching programs. Funds have been utilized for the addition of personnel, for the construction of research and service facilities and for the procurement of extraordinary equipment, particularly in the field of radiotherapy. Also, the university medical center offers a radiotherapist the advantages of expert consultants, prestige and facilities to expedite routine records and follow-up of patients. Favorable as well as many unfavorable

cancer patients are directed to some of these medical centers through reference by doctors and demands by patients. The advantages of such special facilities tend to compensate for the difficulties and frustration encountered in caring for the many recurrent, intractable and terminal cases. It is fortunate when such centers are directed by men of scientific interest and professional integrity who seek no personal advantage and make no exorbitant claims for their medical facilities. The regional radiotherapist engaged in private practice in the vicinity of such a medical center must of necessity compete with its many special facilities, arranged publicity, renowned prestige and its subsidy by philanthropy and government.

There are, on the other hand, trends current in medical practice and social development promoting more complete diagnosis and extensive treatment of cancer in communities of 10,000 to 30,000. In the past, most patients with cancer from these communities have been referred to regional surgeons and radiotherapists in private practice or to the agency hospital providing free medical care. Reference was based on the need for special skill and facilities, attending operative hazards and economic factors. Now, increasingly more communities of 10,000 boast of new or extended hospital facilities providing for major surgery, the consultative service of a regional pathologist and recently of a local certified radiologist equipped for roentgen and radium therapy. Local medical care is further favored by the preference of many patients to remain in their home community for reasons of association, security, convenience and expense. Many low income patients who previously would have gone to the agency hospital providing free medical care are now covered by voluntary prepayment hospital and medical care and can thereby afford private care of their own choice. Our general physicians and surgeons of today, being more extensively prepared and now fortified with better hospital and medical facilities, have become more venturesome in both the diagnosis and treatment of cancer. The ready availability of transfusions for replacement of blood loss and of antibiotics for control of infection have so reduced the operative hazards from mastectomy, hysterectomy and other resective surgery as to encourage more surgery in smaller communities. As a result of these many factors, more patients with early cancer of favorable prognosis are now being treated by surgery and radiation in communities of 10,000 to 30,000.

As is to be expected, patients with more advanced, recurrent and hopeless cancer are still being referred to the famous surgeon, the notable radiotherapist, the renowed clinic, or the agency center providing free medical care. Concentration of such difficult and frustrating case material in the regional center calls for extraordinary facilities, procedures and skills as well as an appreciation of the problems of the local doctor. Reference of patients with cancer is prompted not only to provide optimal medical care but also to share responsibility with accepted specialists for the inevitable complications and failures inherent in the disease. The regional surgeon offers greater prospects in control of resectable cancer through more radical surgery in the chest, abdomen, brain, head and neck as well as those more heroic procedures such as complete pelvic viscerectomy, bilateral adrenalectomy and hypophysectomy for advanced and intractable cancer.

The regional radiotherapist may offer the advantages of special skill and experience, extraordinary facilities and more or less prestige as a consultant. Special radiotherapeutic skills often revolve about the more effective use of intracavitary and interstitial radium, of transcavitary roentgen therapy or of a special individual or group interest in cancer of the mouth, throat, uterus, bladder and other regions wherein possible radiocurability is such as to merit an ultimate effort by the therapist. Extraordinary radiotherapeutic facilities

may be a radioisotope laboratory, a generator of megavoltage radiation, a rotational unit or other special equipment. It is unfortunate that the "C-bomb," the "x-ray cannon" and "atomic medicine" have been so unfairly sensationalized as promising "cancer cures" by our zealous press as to undermine the confidence of patients in conventional radiotherapy and their responsible physicians. To be sure, megavoltage radiation offers limited advantages over conventional 200 kv. radiation: (1) a higher depth to surface dose ratio, (2) less absorption by skin and bone and (3) less radiation sickness. It appears, however, that conventional roentgen and radium therapy properly combined and administered does provide comparable control of most cancer, even though the conventional techniques may be more exacting and time consuming than megavoltage therapy. There is some promise that generators of megavoltage radiation in the form of radiocobalt, linear accelerators or more conventional equipment will eventually become generally available in the highest price range of 250 to 400 kv. equipment. We can all do much to improve our results with conventional radiotherapeutic tools through correlating our efforts to be better clinicians, better radiologists and better physicists.

Facilities for the clinical use of radioisotopes are in the realm of any radiologist who will take the time, trouble and expense to properly train and equip himself or an associate in this field. In our experience, the radioisotope division functions best as an integral part of radiology: (1) to make the consultation and service available to all clinicians in every department, (2) to properly integrate the service with other radiotherapeutic facilities, and (3) to insure physical accuracy through supervission by one trained in radiation physics. The clinical staff as well as the radiologist all enjoy prestige from these added diagnostic and therapeutic contributions to patient care. The almost universally good response of the properly selected thyrotoxic patient to radioiodine is truly an inspiration to the therapist being in particular contrast to the depressing tragic course of too many cancer patients.

A comparative analysis of the changing distribution of work load in the radiology departments of the University of Nebraska Hospital providing free medical care and the Nebraska Methodist Hospital, a private hospital, suggests some trends in current radiologic practice. The University Hospital showed an increase in diagnostic procedures from 1.3 per admission in 1945 to 3.0 per admission in 1949 with slight progressive rise to 3.3 per admission in 1952. Radiotherapeutic procedures per admission have shown little change from 0.70 per admission in 1940 to 0.76 in 1952, the 10 per cent increase resulting from radioisotopic procedures. Radiotherapeutic procedures changed from 10 per cancer case admitted in 1940, through 11 per case in 1945 and down to 8.7 in 1952, indicating a current trend toward relatively fewer cancer cases being treated by radiotherapy. The Nebraska Methodist Hospital showed an increase in examinations from 0.75 per admission in 1945 to 1.25 in 1952 of which 0.25 must be discounted as purely outpatient increment. Radiotherapeutic procedures in private practice have shown an increase from 0.3 per admission in 1940 to 0.75 per admission in 1952 which is essentially an index of growth in private reference from outside the hospital. In both institutions the number of radium applications has been fairly constant during the past five years at about 100 per year, although declining somewhat recently. The radioisotope program has developed progressively during the past five years, radioiodine, radiogold, radiostrontium and radiophosphorus now accounting for about 10 per cent of the total activities of the radiotherapeutic section in both university and private practice.

It seems improbable that the demands for radiotherapy will increase in the near future and may actually decline with the further extension of the surgical treatment of cancer, possible future developments in chemotherapy, and increasing concern re-

garding postirradiation sequelae and complications. To be sure, the incidence of cancer is anticipated to increase about 15 to 20 per cent over a period of ten years from aging of the population. However, the increase is occurring primarily in carcinoma of the bronchus, carcinoma of the prostate and other regions in which benefit from radiation therapy is low, whereas the incidence of cancer of the skin, uterus and breast, in which radiation therapy has been most effective, seems to be on the decline.

Radiologists should seek appointments on the boards of our Blue Cross and Blue Shield prepayment hospital and medical care plans in order to see that radiological services are properly covered and to insure the best interests of the patient. Of 160 million people in the United States, 87 million are now covered by some type of prepayment hospital insurance with 65 million covered for surgical care and 28 million for medical care also. Of these, 42 million are covered by Blue Cross Hospital Service and 25 million by Blue Shield Medical Care Plans. All good voluntary health care plans are worthy of support, but Blue Cross and Blue Shield have the special advantages of hospital and medical direction, of returning a larger percentage of the policy holder's dollar in benefits and they alone offer any prospect of a service contract to the patient. Payments for radiotherapy should always be identified as professional service and must be included exclusively under Blue Shield Medical Care benefits. Unfortunately, diagnostic radiologic services have in some areas been taken over by the Blue Cross as a hospital service, this transgression having been abetted by the indifference and even cooperation of some short-sighted radiologists who would trade professional control for financial convenience. It has been shown that unlimited diagnostic radiologic service even in the hospital is subject to excessive abuse, is not an insurable item and promotes unnecessary hospitalization.

Radiotherapy, particularly when limited to the treatment of cancer, is definitely an insurable service both at the office and in the hospital and as such should be included among the benefits in all surgical and medical care plans. Fees for radiotherapeutic services should be comparable to those for surgical treatment of corresponding disorders. Benefits should be payable in addition to as well as in lieu of surgery, otherwise previous surgery automatically excludes payment for the irradiation of all postoperative recurrences as well as desirable preoperative therapy as in carcinoma of the endometrium. Exclusion of benefits for radiotherapy forces the insured patient to accept surgery even though surgical results are admittedly inferior to radiotherapy as in carcinoma of the cervix or in case radiotherapy can achieve a comparable result with less secondary expense and risk to the patient as in postoperative recurrent thyrotoxicosis treated by radioiodine. In the past, insurance plans have been dominated by surgeons and others who have been reluctant to incorporate equitable benefits for radiotherapy on grounds of lack of actuarial experience. Such experience has now been gained by the California Physicians Service, the Kansas City Blue Shield Plan, the Nebraska Blue Shield Medical Service and others. Statistical data will be made available through the American College of Radiology.

Some comparative payments made by the Nebraska Medical Service for radiotherapy, surgery and diagnostic radiology are presented to show the relatively low cost of radiotherapy in comparison with claims paid for the surgical treatment of comparable conditions and with the rising costs of diagnostic radiology. Total payments for diagnostic radiology by the Nebraska Medical Service have increased from 2.95 per cent of earned income in 1948 up to 6.35 per cent in 1953.

Review of the Nebraska Medical Service experience shows that payments for essential radiotherapy in cancer of the uterus amounted to only one-fortieth of the fees paid for miscellaneous operations on the uterus and cervix of which many were

TABLE I

COMPARATIVE PAYMENTS FOR RADIOTHERAPY, SURGERY AND DIAGNOSTIC RADIOLOGY
Nebraska Medical Service, 1952

Assignment of Funds	Amount	Per Cent of Earned Income
Cancer uterus, radiotherapy	$ 3,625	0.17%
Hysterectomy and hysteropexy	105,270	4.94
"Fibroids," radiotherapy	958	0.045
Cervix—conization, cautery	21,472	1.01
Cancer skin, radiotherapy	2,130	0.10
Skin tumors, surgery	22,214	1.04
Radiotherapy, total	26,610	1.25
Surgery, total	1,137,940	52.25
Diagnostic radiology, accident	69,813	3.27
Diagnostic radiology, in hospital 4 days	42,237	1.98
Diagnostic radiology, with surgery	17,057	0.80
Diagnostic radiology, total	128,907	6.05
Total payment for claims	1,746,188	81.89
Administrative expense	197,434	9.26
Added to reserves	188,710	8.85
	$2,132,332	100.00%

elective procedures of questionable merit and urgency. Tumors of the skin showed payments for surgical removal to be ten times those for radiotherapy.

Payments for radiotherapy under the Nebraska Medical Service Plan are restricted to certified radiotherapists under whom are included not only radiologists but also other certified specialists who can show satisfactory evidence of qualified training in radiotherapy. Benefits for radiotherapy under the Nebraska Plan are confined to malignant neoplasms, blood dyscrasias, hemangiomas, hyperthyroidism and abnormal uterine bleeding for which the total payments covering all radiotherapy including roentgen ray, radium and radioisotopes amount to only 1.25 per cent of the earned income (see Table 1).

The Kansas City Blue Shield Plan pays about 2.5 per cent of its earned income for radiotherapy of which over 60 per cent is paid for nonmalignant diseases. In our opinion, it is more important to adequately finance the treatment of cancer and comparable major diseases than to dissipate radiotherapeutic insurance benefits on minor dermatoses and bursitis. Substandard benefits for radiation therapy are worse than none, particularly under a service contract. In case the fees for radiotherapy are inadequate, the radiologist can hardly afford to sign as a participating physician since under the service plan he agrees to accept these inadequate fees in total payment for services rendered. The allowances for proper combined treatment of carcinoma of the endometrium and carcinoma of the cervix uteri by roentgen therapy and radium are definitely substandard in the Kansas City and Nebraska plans. Insurance, like other forms of socialism, tends to undercompensate those workers who accept the challenge of the arduous task or difficult assignment and strive toward optimal accomplishment.

The radiotherapist has the responsibility to participate in the organization and activities of those agencies which concern themselves with the problem of cancer. Of the 24 doctors now on the Board of Directors of the American Cancer Society, 2 are radiologists, one of whom, Dr. A. M. Popma, is currently President. Among the

TABLE II

ANALYSIS OF TOTAL PAYMENTS FOR RADIOTHERAPY
Nebraska Medical Service, 1952

Lesion	Services	Payments	Per Cent of Earned Income
Cancer of breast	60	$ 6,765	0.32%
Cancer of uterus	29	3,625	0.17
Cancer of skin	54	2,130	0.10
Lymphomas	20	1,490	0.07
Brain	11	1,225	0.06
Fibroids	12	958	0.05
Cancer of lip	17	846	0.04
Hyperthyroidism	11	820	0.04
Cancer of nasopharynx	8	815	0.04
Hemangiomas	46	569	0.03
Miscellaneous	71	7,367	0.35
Total	339	$26,610	1.25%

79 coordinators of cancer teaching in our medical schools 7 are radiologists, 37 are surgeons, 24 pathologists, 7 internists and 4 other specialists. The radiotherapist should accept appointment to the local board of the American Cancer Society, to the cancer committees of his county and state medical society and he should serve on the tumor boards of his hospital staff and medical school. He has an obligation to participate in these activities, both to gain orientation in the programs as well as to aid in their intelligent direction.

The development of group practice is strengthening the status of radiology as a specialty. In group affiliation the individual necessarily surrenders some of his personal prerogatives but benefits in turn from pooling of resources, subdivision of responsibilities and delegation of certain nonprofessional details. In clinic group practice the radiologist may be an essential and valued member of a professional team composed of general practitioners and specialists, an increasingly common arrangement in communities of 10,000 to 30,000. In larger communities, a more common affiliation is among specialists in a single field such as a group of radiologists. The young radiologist entering a specialist group profits from an assured income with assigned responsibilities, prestige of an established practice, the guidance of experience and maturity and progressive advancement with eventual participation in a partnership. All members profit from mutual opportunities for attendance at meetings, postgraduate courses and vacation schedules. Senior members can more securely finance expensive equipment and expand facilities since their commitments are protected through the perpetuation of practice and solvency of the group. High income taxes make it advantageous to spread income more evenly over a period of years and to avoid overly oppressive loads of individual work with excessively burdensome responsibility.

No one physician can hope to be fully competent in all aspects of the diagnosis and treatment of cancer, covering as it does nearly all the specialties and subspecialities in medical practice. The omniscient cancer specialist is either a genius or a fraud. Allotment of responsibility for the treatment of cancer is primarily according to the regional specialty concerned or according to the surgical, medical or radiological modality applied. Designation of the cancer expert is an individual consideration peculiar to the particular problem of the patient and the interests and capa-

bilities of the doctors regionally available. If therapy is primarily surgical, certainly the surgeon should be in charge. If therapy is primarily radiologic, the radiotherapist should accept full responsibility for management during that period of treatment. To be sure, the radiologist like other physicians will benefit his patient and relieve personal pressure by appropriate consultation. Consultation is to be sought whenever the problem gets beyond his limited capabilities, whenever alternate programs of therapy are to be considered and whenever a crisis develops or dissatisfaction is suspected in the patient or his family. All radiotherapeutic departments should have their own clinical service and beds the same as other clinical departments responsible for definitive care. The therapeutic radiologist must be primarily a clinician who utilizes radiation and chemotherapy as a surgeon uses a scalpel. The radiotherapist, and in fact all physicians, must be made to feel responsible for the palliative and terminal care of patients with incurable cancer. With modern facilities we can now offer the incurable patient worthwhile benefit in the relief of pain, control of infection, combat of toxemia, replacement of blood and maintenance of nutrition. We must not abandon the suffering patient and his distressed family regardless of how frustrated and inadequate we may feel as physicians.

In summary, the status and practice of radiotherapy, particularly as applied to cancer, is being molded by diverse political, social, scientific and economic influences. On the one hand, radiology in communities of 10,000 to 30,000 is enjoying an expanded role in the field of conventional therapy of selected cases. On the other hand, cancer cases now referred on to the regional radiotherapist are increasingly difficult and intractable calling for a broadening of facilities and enhancement of skills. All radiotherapists are urged to make optimal use of intracavitary and interstitial radium as well as roentgen therapy, to consider the development of a radioisotope program at this time and to currently watch developments in megavoltage therapy. Today the private radiotherapist must compete with the subsidized facilities for cancer therapy offered by some privileged medical school centers, the Veterans Administration, and state cancer hospitals. It seems improbable that current demands for radiotherapy will be exceeded for some time, considering the restriction of suitable case material, aggressive extension of radical surgery for cancer, unfulfilled hopes for chemotherapy in cancer and increasing general concern as to postirradiation sequelae. Radiologists practicing as a group can benefit from pooling of resources, subdivision of responsibilities and mutual aid in professional problems. Prepayment medical care insurance is a potent force in the preservation of private practice. Benefits for radiotherapy in cancer, hyperthyroidism and other major diseases are definitely insurable and adequate payments should be provided in all medical prepayment contracts. Radiotherapists should participate in the organization and activities of the various cencer agencies both to gain orientation and to aid in direction of these important programs. The radiotherapist is primarily a clinician whose status as a consultant must be established on the basis of a broad understanding of cancer and allied disease embellished by his special knowledge and skills in radiology.

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SURGICAL AND RADIOLOGICAL RESULTS IN THE TREATMENT OF ESOPHAGEAL CARCINOMA*

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SEATTLE, WASHINGTON

ONLY during the last decade have both surgical and radiological techniques been developed which could theoretically promise more consistent and functionally more satisfactory results in the treatment of carcinoma of the esophagus. The development of thoracic surgery, aided mainly by improved methods of anesthesia and control of shock and infection, permitted the systematic elaboration of subtotal esophagectomy with intrathoracic esophagogastrostomy in one stage with more adequate removal of the regional lymphatics and restoration of continuity to a more nearly normal functional status. The availability of better radiation facilities and the elaboration of more adequate techniques—the use of rotation or multiple perithoracic ports and supervoltage radiation—made possible the introduction of sufficiently high and homogeneous doses such as are considered necessary for the sterilization of a tumor of the biological type of mucosal epidermoid carcinoma.

These methods—both surgical and radiological—are still in flux. Experience and skill have increased during the last five years and an assessment based on an evaluation of five year results obtained in patients treated prior to 1946 must therefore be made with reservation. Yet it appears worth while to pause at this stage and to attempt an evaluation of what so far has been accomplished by surgery and radiation therapy in an effort to reach—if possible—at least some tentative indications with regard to the preferable procedure in the individual situation. On reviewing the literature we are impressed by the lack of appreciation in either field for the accomplishments and limitations of the other method. In many radiological publications, particularly in the European literature, surgical results still are discussed as unpredictable curiosities which do not deserve serious consideration in the evaluation of indications for treatment in individual instances. Conversely, we find in the American surgical literature either a complete disregard of the possibilities of radiation therapy or a derogatory attitude such as that expressed as recently as 1951 by Wangensteen in the small monograph on "Cancer of the Esophagus and Stomach" distributed by the American Cancer Society: "In a few areas, there is still a remnant of enthusiasm for roentgen ray treatment." Nowhere is any serious attempt made to evaluate whether a correlation of surgical and radiological results could lead to a better selection of cases for either procedure which may improve the so far pathetic over-all picture.

In order to make a comparison of surgical and radiological results reasonably useful, certain requirements must be met.

1. We must talk about the same disease, namely epidermoid carcinoma.

2. The material must be sufficiently large to be meaningful.

3. The material must be composed of reasonably comparable cases in regard to the stage of the disease.

4. Cancers originating in different levels of the esophagus present different therapeutic problems for both surgeon and radiotherapist and should therefore be considered separately. We follow the suggestion of Sweet who recognizes four segments of the esophagus: a cervical segment (extending from the level of the lower margin of cricoid cartilage to the thoracic inlet), and a thoracic segment, the latter subdivided into an upper fourth, middle half,

* Presented at the Thirty-fourth Annual Meeting, American Radium Society, Chicago, Ill., June 8–10, 1952.

and lower fourth. The middle half is again subdivided at a point several centimeters below the inferior margin of the aortic arch because of the different surgical prognosis, depending on the necessity of a supra-aortic or infra-aortic anastomosis.

CERVICAL ESOPHAGUS

For anatomical reasons, chances for successful surgery increase and the primary surgical risk decreases from the cervical area downward. Surgical removal of cancers originating in the cervical portion of the esophagus which comprise about 10 per cent of esophageal cancers has so far been quite disappointing. They necessitate complicated multiple stage procedures. While the functional result apparently can be satisfactory, prolonged survivals have been reported in sporadic instances only. Watson and Pool report in 1948 from the Memorial Hospital 7 cases in which resection of the cervical esophagus could be carried out between 1940 and 1947. Only 1 patient was alive without symptoms seven years later. At the time of the report, 3 patients were well for less than one year, 2 were alive with active recurrences. There was 1 surgical mortality. Sweet has used the Wookey procedure in 7 instances with excellent immediate results but with either local recurrence or lymph node extension in every case within one year. He summarizes: "In the neck and in the superior mediastinal segment, even though in favorable cases a safe margin might be obtained on the esophagus itself, it is virtually impossible to remove a sufficient number of regional lymph nodes in continuity with the primary growth. The results of surgical extirpation in this group of cases are exceedingly unfavorable."

It is difficult to find reports in the radiological literature in which lower hypopharyngeal lesions and those originating in the cervical esophagus are clearly enough separated for evaluation. But since the inclusion of low hypopharyngeal carcinomas would rather aggravate statistically poor results than improve them (because of the inclusion of the unfavorable lesions involving the cricoid cartilage), certain conclusions, even without sharp separation of these groups are probably permissible. In a group of 56 cases of such low hypopharyngeal lesions treated at the Radiumhemmet between 1943 and 1945, symptom freedom after five years was reported by Jacobsson in 10 cases, or 17 per cent. In our own group of 12 cases of carcinoma of the cervical esophagus treated between 1939 and 1951, 2 are well and without symptoms for eight and ten years respectively. One of these had considerable roentgenographically and microscopically demonstrable direct paraesophageal extension.

Because of the better accessibility of these lesions which facilitates the introduction of an adequate tumor dose compared to those in the thoracic esophagus, the likelihood of radiological control of the *primary lesion in the esophagus and its direct extension in the surrounding soft parts* is probably at least as good as the likelihood of complete surgical removal. Extension of the disease into lymph nodes can probably not be controlled by either surgery or radiation therapy with any degree of consistency. Surgery is admittedly unable to remove the involved lymphatic area en bloc. For reasons to be discussed later, it is unlikely that radiation therapy will offer any better chance of control in lymph nodes. But radiation therapy probably offers better chances of prolonged temporary palliation and retardation by causing fibrosis of these nodes even if they are not sterilized. The morbidity due to the treatment itself in patients in whom only palliative results can be accomplished is considerably less than that caused by the type of surgery necessary in this situation.

Thus, it would seem that in the treatment of lesions in the cervical segment, radiation therapy has preference as long as surgery cannot offer more consistent permanent results.

LOWER FOURTH OF THORACIC ESOPHAGUS

Carcinomas in the lowermost segment of the esophagus comprise about 13 per cent of epidermoid esophageal carcinomas. I

have not been able to find radiological or surgical statistics in which these tumors are sufficiently separated as a group from either epidermoid carcinomas in the higher portions of the esophagus or adenocarcinomas of the cardia, but even in the absence of reliable statistical evidence, it would seem, on the basis of general considerations, that surgery should have preference in the treatment of cancers originating in this portion of the esophagus.

These lesions tend to involve the cardia and to spread more frequently into the subdiaphragmatic abdominal lymph nodes. Adequate irradiation over such large areas is therefore more problematic than for the better defined lesions in the upper thoracic portion of the esophagus. With surgical exploration the presence of regional nodes below the diaphragm is at least recognized and in a number of instances the nodes have apparently been successfully removed with the primary lesion. The surgical results obtained in this portion of the esophagus are considerably better and the primary mortality markedly lower than for lesions in the thoracic portion (see Sweet's comparison in Tables II-V). While the surgical statistics do not exclude adenocarcinomas originating in the cardia, it seems that the reported results in general can still be considered as a reasonably reliable guide. Sweet has accomplished 14.8 per cent five year results in 74 patients in whom resection was possible, or in 11 per cent of 100 patients explored, compared to 3.3 per cent and 2.5 per cent for the respective groups of carcinomas in the mid-thoracic portion; with a primary surgical mortality of 11 per cent in lower fourth resections as compared to 24 per cent for lesions in the upper three-fourths.

Paradoxically the longest symptom-free survival in our own group of epidermoid carcinomas of the esophagus treated by irradiation was observed in a patient with a tumor in this lower segment. But surgery of cardia and lower esophagus by transthoracic approach has so much improved during the twelve years since this patient was treated that today he would undoubtedly be considered as a candidate for surgery although at that time surgery was refused by one of the outstanding surgeons in the country.

UPPER AND MIDDLE SEGMENTS OF THORACIC ESOPHAGUS

This group represents numerically the most important one. Carcinomas located in the upper fourth comprise about 7 per cent and those in the middle half about 70 per cent of esophageal cancers.

For the purpose of comparison, I have selected the surgical statistics by Sweet and Garlock and the radiological results reported by Nielsen (Radium Center, Copenhagen); Gynning (King Gustaf V Jubilee Clinic, Lund, Sweden); Smithers (Royal Cancer Hospital, London); and Watson (Saskatoon Cancer Clinic). I have attempted to clarify the situation as much as possible and to bring the results up to date by personal correspondence, and I wish to thank Doctors Sweet, Garlock, Nielsen, Smithers, and Watson for their cooperation

As previously pointed out, it is difficult to find larger surgical and radiological series composed of reasonably comparable material with regard to the stages of the diseases admitted for therapy. In this regard it is fortunate that Sweet regards palliative resection as indicated even in instances in which radical removal of the disease cannot be expected. He therefore submitted a larger number to exploration and resection than Garlock who does not adhere to the philosophy of palliative surgery in the presence of uncontrollable disease. Thus Sweet's material is more comparable to that accepted for radiation therapy: Of all his patients seen, 86 per cent were explored as compared to Nielsen's group in which 90 per cent of the patients seen were admitted for treatment. For this reason, Sweet's material which represents a large number of patients consistently and most expertly treated and adequately followed, was used for comparison with the radiological results. In order to make the statistical evaluation more meaningful and because survivals after different periods of

TABLE I

CARCINOMA OF THORACIC ESOPHAGUS*
Per Cent Symptom Free

	Of All Patients Treated		Of Patients "Sufficiently" Treated	
	Surgery (Sweet)	Radio-therapy	Surgery (Sweet)	Radio-therapy
1 yr.	36.8 (46:125)	33 (20:60)	48.5 (46:95)	42.5 (20:47)
2 yr.	13.1 (15:114)	11.6 (7:60)	17.2 (15:87)	14.9 (7:47)
3 yr.	9.7 (9:92)	6.8 (18:262)	12.9 (9:70)	10.4 (18:173)
5 yr.	2.5 (1:40)	3.6 (8:218)	3.3 (1:30)	6.2 (8:128)

* Details from which this synoptic table was constructed are given in Tables II, III, IV, and V.

time were not reported in all individual radiological publications, I have pooled the radiological results reported by the four centers previously mentioned. I believe that this presentation of pooled material is justified since the results obtained in different radiological centers of equal competence were quite comparable.

In Table I a synopsis of the results obtained by surgery (Sweet's material) and radiation therapy is presented. The details from which this synoptic tabulation was calculated are given in Tables II, III, IV, and V.

Percentages of survival without clinical symptoms or demonstrable active disease were calculated separately for all patients who were accepted for treatment and for those in whom treatment could be satisfactorily concluded. Thus, the first surgical group comprises all patients explored and the second one all those in whom resection was done (including those who did not survive the operation). The first radiological group includes all patients who were accepted for radiation therapy regardless of whether treatment could be concluded and carried to such a dose that a permanent or prolonged palliative result could be expected. The second group represents those in whom treatment could be concluded as originally planned and a minimal tumor dose of a level now considered adequate (5,000 r in thirty-five to forty days or its equivalent with different protraction in time) could be introduced.

Five Year Symptom Freedom (Thoracic Esophagus). The table would indicate that if *approximately comparable clinical material without too careful selection of patients is compared, the results obtained by equally competent surgery and radiotherapy are in the same range.* Five year symptom freedom was accomplished in between 3 and 6 per cent of the cases adequately treated. I do not believe that too much emphasis should be placed on this small difference in percentage considering the rather small number of cases and the other pitfalls inherent in such analysis. We should, however, emphasize that in spite of the apparent comparability of the material, as previously discussed, still the radiological series probably includes cases that would have been rejected even for exploration by Sweet. Of Nielsen's 194 cases (of which 174, or 90 per cent, were treated) there were 141, or 72 per cent, with lesions more than 5 cm. in length as measured on the roentgenogram; 67 of which, or *34 per cent of the entire material, were more than 10 cm. in length.* Fleming has shown on autopsy material that the incidence of lymph node involvement in lesions up to 5.1 cm. was 50 per cent while this figure increased to almost 90 per cent in lesions beyond that length. Sweet reports that in 174 cases in which the lymph nodes were studied, only 57.5 per cent showed involvement, which would indicate that his material was more favorable than that in the radiological series. Thus, we can assume that about one-third of the patients still accepted for radiotherapy would probably have been considered inoperable prior to exploration because of the size of the lesion. If that is correct, the apparently similar results of surgery and radiotherapy as they appear in the tabula-

tion would actually indicate statistical superiority of radiation therapy, if rather unselected material is analyzed.

In evaluating the material, it should furthermore be considered that experience and skill have increased during recent years. This may—at least theoretically—improve results obtainable now and in the future beyond those tabulated which were obtained in patients treated more than five years ago. Considering, however, the incidence of failures already apparent in patients treated by both surgery and radiotherapy more recently than five years ago, it is unlikely that a dramatic statistical improvement for a similar rather unselected material can be expected by increase in experience and technical skill only. This is understandable considering the nature of the disease, its relatively late recognition and its tendency to early extension beyond the organ primarily involved. The bogeyman of earlier diagnosis, of course, always enters such discussion but, in the majority of cases, this is not likely to change markedly the over-all situation. From an analysis of 170 cases, Parker *et al.* recently concluded that the preoperative duration of symptoms did not influence the rate of operability. They found a history of less than three weeks' duration in 17 per cent, yet the majority of these patients with very recent symptoms were found inoperable or unresectable. This would again support Macdonald's contention of the "biological pre-determinism" as an important factor in prognosis. Macdonald could demonstrate in a number of common forms of cancers that the short history (or "early" recognition) does not necessarily imply the better prognosis. On the contrary, cancers with a long history may be of the slower growing and biologically more favorable type. While this does not intend to minimize the importance of early diagnosis, it makes it unlikely that diagnostic improvement will appreciably change the statistical prognosis and results of treatment.

More important improvement can be expected from a more careful selection of patients. This is suggested by the better statistical results obtained by Garlock. As previously mentioned, his material is more rigidly selected, as expressed by his resectability of only 46 per cent of all patients explored as compared to Sweet's 76 per cent. Garlock, up to November, 1950, reported 10 patients symptom free for more than five years out of 36 patients resected, or 28 per cent; or 12 per cent of all 81 patients explored.

More careful selection of patients for surgery will of course improve only the relative cure rate of those patients in whom resection is done. Theoretically, it will not improve the absolute cure rate of all patients seen. But it is interesting to note that the over-all cure rate of all patients explored in Garlock's series is actually superior to Sweet's. This would imply that more careful selection of patients should accomplish the same over-all results, but would save many patients the ordeal of ineffective surgery.

In an attempt to find more definite guides for the selection of patients for either surgery or radiation therapy, it is essential to analyze the reasons for the consistently low incidence of successes and for the overwhelming incidence of failures by both surgery and radiotherapy.

Surgical removal or radiological control of the *primary lesion*, as long as it has not extended beyond the esophageal wall, can probably be accomplished with approximately the same degree of consistency. Roentgen-ray doses sufficient for sterilization of this type of tumor in its primary site, if introduced with modern technical facilities and with sufficient skill, have produced control of the primary lesion in a higher number of cases than remained clinically altogether controlled. In addition to the small number of those patients in whom the disease remained clinically and radiologically controlled for more than five years as shown in Table 1, autopsies of patients, who died of progressing disease outside of the esophagus or of other causes, have demonstrated the absence of disease

TABLE II

CARCINOMA OF ESOPHAGUS

Symptom Free Survival after 1 Year

	I No. Treated	II No. Sufficiently Treated	III No. Well	IV Per Cent Well of I	V Per Cent Well of II
Sweet up to 1949					
Mid-thoracic	(125)	95	46	36.8	48.5
Lower thoracic	(181)	138	66	36.4	48.7
TOTAL	(306)	233	112	36.6	48
Smithers	44	32	14	31.8	43
Watson	16	15	6	37.5	40
TOTAL	60	47	20	33	42.5

TABLE III

CARCINOMA OF ESOPHAGUS

Symptom Free Survival after 2 Years

	I No. Treated	II No. Sufficiently Treated	III No. Well	IV Per Cent Well of I	V Per Cent Well of II
Sweet up to 1948					
Mid-thoracic	(114)	87	15	13.1	17.2
Lower thoracic	(172)	131	35	20.4	26.7
TOTAL	(286)	218	50	17.4	22.9
Watson	16	15	2	12.5	13.3
Smithers	44	32	5	11.3	15
TOTAL	60	47	7	11.6	14.9

Tables II, III, IV, and V. Carcinoma of esophagus. Symptom-free survival after 1, 2, 3, and 5 years.

Column I represents all patients admitted for either surgical exploration or radiation therapy regardless of whether either resection could be done, or whether radiation therapy could be completed. Sweet does not report the number of patients actually admitted for exploration but only those in whom resection was done. On the basis of his reported resectability of 76 per cent of all explored patients, the number of explorations was calculated and appears therefore in parentheses.

Column II represents those patients that were "sufficiently treated." This means, in whom either resection was done, or radiation therapy could be completed with an adequate tumor dose of at least 5,000 r in 30 to 35 days, or its equivalent.

Column IV represents the percentage of patients alive and free of symptoms after 5 years, of all those who had been admitted for treatment (Column I).

Column V represents the percentage of all patients alive and free of symptoms after 5 years of those who had been "sufficiently treated" (Column II).

The percentages of Columns IV and V were calculated on the basis of the absolute numbers (Column II and III) as reported by the respective authors. Since some of the authors did not report these percentages themselves because they used different standards for calculation, they do not always represent the percentages as found in the respective reports. Sweet, for instance, does not calculate percentage of all patients explored or resected, but the percentage of those patients who had "an opportunity to survive," *i.e.*, after deduction of primary mortality. In order to make the material comparable with radiological material, it was necessary to express cure rates in the manner here used.

Not all authors have given their results after 1, 2, 3, and 5 years. For this reason, the material of each author does not necessarily appear on each one of these tables.

Table IV

CARCINOMA OF ESOPHAGUS

Symptom Free Survival after 3 Years

	I No. Treated	II No. Sufficiently Treated	III No. Well 5 Yr.	IV Per Cent Well of I	V Per Cent Well of II
Sweet up to 1947					
Mid-thoracic	(92)	70	9	9.7	12.9
Lower thoracic	(130)	109	25	19.2	23
Total	(222)	179	34	15.4	19
Gynning 1943–1947	88	77	8	9	10.3
Nielsen 1941–1943	174	96	10	5.7	10.4
Total	262	173	18	6.8	10.4

Table V

CARCINOMA OF ESOPHAGUS

Symptom Free Survival after 5 Years

	I No. Treated	II No. Sufficiently Treated	III No. Well 5 Yr.	IV Per Cent Well of I	V Per Cent Well of II
Sweet up to 1945					
Mid-thoracic	(40)	30	1	2.5	3.3
Lower thoracic	(100)	74	11	11	14.8
Total	(140)	104	12	8.6	11.5
Nielsen (1941–1943)	174	96	5	2.8	5.2
Smithers (1937–1939)	44	32	3	6.8	9.3
Total	218	128	8	3.6	6.2

in the treated portion of the esophagus more frequently than would be consistent with chance. In Watson's series, 5 out of 7 autopsies showed no evidence of recurrence in the esophagus (3 of these died of cardiac failure). Smithers in his group of 32 completely treated patients observed 3 instances in which at postmortem no sign of residual tumor or ulceration was found, in addition to the 3 patients who were free from symptoms for more than five years (Table I). In 4 additional cases, local ulceration but no viable cancer was found at postmortem and 6 more patients died without return of symptoms. This would suggest that in 16 out of 32 adequately treated cases the primary lesion was controlled. Likewise Nielsen, in addition to those patients included in the tabulation, observed 8 deaths (probably all due to meta-

static disease) between the second and fifth years without sign of local recurrence.

Thus, there can be no doubt that, with adequate treatment, the primary focus in the esophagus can be controlled with considerable consistency. As in all epidermoid carcinomas, we must assume that there is probably a certain small number of esophageal carcinomas in which the primary focus will remain uncontrolled for unexplained reasons, in spite of an adequate dose delivered. If we judge the probable incidence of this occurrence from experience with other epidermoid carcinomas, such as those of the cervix , it is sufficiently low to be far outweighed by the operative surgical mortality if for this reason alone surgery would be favored in all but inoperable lesions.

The old objection that, because of the thin wall of the esophagus, control of the carcinoma cannot be accomplished without perforation does not hold true if the treatment is given with due consideration of the particular type of tumor and close attention to signs and symptoms indicating the danger of perforation. In a small number of instances such perforation is probably inevitable because of the type and extent of the tumor, but in these cases (which represent the large ulcerating and disintegrating tumors) surgery usually will likewise fail.

Direct extension of the tumor through the esophageal wall with fixation to the mediastinal structures or vertebrae makes curative surgical removal impossible. Whether radiation therapy occasionally could control direct extension remains to date a matter of speculation. Experience with other tumors has taught us that direct extension of epidermoid carcinoma can at times be controlled while lymph node deposits cannot. This would make it reasonable to subject patients to radical radiation therapy who for this reason are found inoperable at exploration even if the likelihood of success is small.

The main reason for the high incidence of failures is the tendency of esophageal carcinoma to spread early throughout the rich lymphatic network of the esophageal wall with *deposits in the intramural lymph nodes* along the esophagus *and in the paraesophageal and mediastinal lymph nodes*. Since the intramural spread may extend along the entire length of the esophagus, any procedure, surgical or radiological, that includes only part of the organ, is apt to leave active disease.

It is likely that the involvement of regional lymph nodes with very few exceptions demarcates the border line between curability and incurability by either surgery or radiation therapy. We are unable to control lymph node involvement secondary to epidermoid carcinoma of the oral cavity (with the exception of some highly anaplastic lesions) by external irradiation. It has been pointed out that the incidence of demonstrable lymph node involvement found at surgery in different stages of carcinoma of the cervix parallels so closely the percentage of radiological failures in these respective stages as to suggest that permanent radiological results are accomplished only in instances with direct parametrial extension but not in the presence of lymph node involvement. On the basis of these experiences with similar types of carcinoma, it is unlikely that radiation therapy will be able to control lymph nodes secondary to esophageal carcinoma with any degree of consistency.

Whether surgery can accomplish more in this respect cannot be decided from the material so far available. It is possible that in the presence of minor lymph node involvement, surgery in a certain number of instances may succeed in eradicating the entire disease. The sharp drop of curability in the presence of lymph node invasion is well recognized in other cancers such as those of the breast and tongue. For carcinoma of the esophagus, I have not been able to find factual evidence as to the actual salvage in the presence of demonstrably involved lymph nodes that would stand critical analysis.

Thus, it would seem that the biological nature of the disease limits the likelihood of improving permanent results by mere

improvement of technique and skill sufficiently to express itself in the over-all five year salvage. Merendino and Mark have calculated the potential surgical five year salvage based on an analysis of 100 consecutive cases. Taking the likelihood of death from other causes in this age group and the primary surgical mortality into consideration, they calculate a maximal cure rate of 20.4 per cent if cases with regional lymph node involvement are still included in the theoretically curable group. If those with lymph node involvement are excluded, a maximal potential cure rate after five years of 15.6 per cent can be calculated. This does not yet take into consideration that an additional but indefinite number of patients used for this study would have been rejected for surgery because of concomitant disease processes and that in the routine autopsies which constitute the background of their calculations, some instances of microscopic or microanatomic lymph node involvement might have been overlooked. Thus, the assumption of a five year potential salvage of 15 per cent is probably rather too high than too low.

PALLIATIVE TREATMENT

For the overwhelming number of patients with esophageal carcinoma, the problem remains that of palliation. At the meeting of the American Association of Thoracic Surgery in May, 1952, Ravitch *et al.* stated in summary that "the results of extirpation of carcinoma of the esophagus to date have been so discouraging as to raise serious question concerning the value of direct attack." Perhaps we should in this particular type of cancer reorient our outlook and to a degree relax in our emphasis on "cure" at any price. This does not mean that every reasonable attempt at permanent control should not be made. But cancer of the esophagus is mainly a disease of the older age group with an average age of around sixty and with the majority of patients in the sixth and seventh decade of life. The life expectancy therefore is in general, apart from the esophageal carcinoma, relatively short compared to that of many patients with other forms of cancer. Restoration even of temporary comfort is therefore of greater significance.

The specific purpose of palliation in this type of cancer is of course the prevention of the misery of starvation. Gastrostomy has in general been abandoned as unsatisfactory. It prolongs life without comfort and happiness. As Roberts has stated in 1936, "Gastrostomy . . . certainly achieves its object up to a point but still leaves the patient in a state of 'withering undelight.' For eating, apart from being a necessity is the greatest of earthly pleasures. This gone, life is not worth living." Insofar as most of these patients—male or female—are in or beyond the menopause, the bowel movement is probably the only true competitor for earthly pleasure. Since the results of resection are poor and the primary risk great a number of shunting techniques including intra- or antethoracic esophagojejunostomy have been suggested. It is remarkable how little the consistent palliative results obtainable by adequate roentgen therapy, with comparatively little discomfort, are recognized and appreciated in the surgical literature.

Restoration and maintenance of oral feedings could already be accomplished in about 50 per cent of patients treated with radiation in the medium voltage range without rotation (Zuppinger, 1936). With rotation therapy, and using medium voltage roentgen rays, Nielsen reports that complete or nearly complete primary freedom from symptoms (almost normal deglutition and radiological improvement of the passage) was obtained in 117 out of 174 patients treated, or in two-thirds of the total number, or four-fifths of the adequately treated patients. In many instances the patients were able to swallow up to the time of death which in most cases was due to metastases and cachexia.

If we compare the number of patients who have survived one, two, and three years following surgery and radiotherapy

(Table 1), either procedure seems to accomplish statistically quite comparable results. It is not likely that patients who died within this period of time following radiation therapy would have lived longer or more comfortably had they been treated surgically. But surgery would have caused them more misery and discomfort. The morbidity associated with even as massive irradiation as is necessary to accomplish sustained palliation is undoubtedly considerably less than that associated with any of the surgical procedures available. With treatment in the medium voltage range, it was at times difficult to conduct treatment without causing constitutional effects. At times it has been necessary to discontinue treatment because the patient's general condition would not support this drastic therapy. Radiation in the million volt range is better tolerated because the total irradiated volume is smaller. Treatment therefore involves less strain for the patient. Discontinuation of therapy on account of the general condition is now rarely necessary. According to Nielsen's experience, the same is apparently true if rotational technique is used with medium voltage irradiation.

Thus it does appear that in instances in which palliative results only can be expected, radiation therapy should have preference over any type of surgical procedure. At times it will be impossible to predict prior to treatment whether permanent control will be possible. In these instances, of course, every effort should be made to accomplish this by either surgery or radiation therapy but when deciding on the procedure in such instances, the curative and palliative results obtainable and the morbidity associated with either procedure should be carefully considered.

INDICATIONS FOR SURGERY OR RADIATION THERAPY

The main factors which guide us in the selection of either surgery or radiation therapy in the individual situation are the biological type of the tumor, its location in the particular segment of the esophagus, and the patient's age.

As in other carcinomas originating in individual organs, certain types of epidermoid carcinomas of the esophagus are by reason of their biological behavior more suitable for surgery or irradiation. The majority of these tumors are histopathologically of a moderate degree of differentiation. Detailed attention to histopathological grading will not give us any more lead than it does, for instance, in carcinomas of the cervix, perhaps with the exception of very anaplastic tumors which are obviously poor objects for surgery; but these are equally uncontrollable by radiation therapy because of their early rapid spread. *The gross appearance of the lesion as seen roentgenographically* gives us, I believe, a more reliable lead. In this respect we can recognize three main types.

1. *Primarily Constricting Circular Lesions.* They may be relatively short at the time when they cause obstructive symptoms and may still be limited to the esoageal wall. This makes them more favorable both from the point of surgical resection as well as radiological sterilization. In a relatively young patient with this type of carcinoma, located in a surgically more favorable segment where therefore the primary operative risk is not excessive, exploration with the intention of radical removal if possible, is indicated if careful preoperative investigation does not reveal any sign or symptom of extension beyond the esophageal wall such as mediastinal or paraesophageal lymph node involvement, phrenic or recurrent nerve paralysis, cough, persistent pain or the roentgenographically demonstrable presence of a niche indicating deeper penetration. While radiation therapy can control this type of lesion in its primary location with a certain consistency, surgical resection may possibly accomplish this with greater probability. As previously mentioned, we find in every type of epidermoid carcinoma a certain small percentage of instances in which such control is not accomplished in spite of adequate

treatment, for unrecognized reasons apparently inherent in the irradiation response of this particular tumor. Minor lymph node involvement may also possibly be surgically controlled when radiotherapy would fail. For these reasons, I would believe that in such situations surgery should be attempted. If such a lesion is located, however, in a segment of the esophagus unfavorable for surgical resection and where surgery would be associated with a high primary risk, either because of the location or the age or general condition of the patient, radiation therapy should be more seriously considered. I may mention here that, if it fails, surgery is still possible. This was done in one of our patients and in spite of the preceding heavy irradiation, no particular surgical complications during or after the resection were encountered. It was always puzzling to me why this type of lesion—while it does not respond as easily as the second, exophytic type and apparently requires a larger dose—can be controlled in spite of the involvement of the esophageal muscle which we must assume to be present in this hard infiltrating type of growth. For most carcinomas—larynx, bladder—involvement of muscle makes the radiocurability much more problematic.

2. *The Exophytic Carcinoma.* These carcinomas form soft exophytic masses and produce large filling defects but considering the length of the lesion, they cause comparatively little stenosis. But because of the late appearance of obstructive symptoms, they are more likely to have spread along the esophageal lymphatics and into the regional nodes in spite of their primarily more exophytic type of growth. For this reason they are less likely to be controlled by either surgery or radiation therapy. This consideration should in doubtful cases weigh against surgery. Essentially these lesions are more responsive to irradiation than the first group. While good palliative temporary results by radiation therapy can be expected if the treatment is given slowly enough to avoid too rapid break-down of the tumor with perforation, permanent radiological results are not likely because of the extra-esophageal extension. In this type, therefore, every factor such as location in the particular segment, age, and operative risk should be carefully taken into consideration, but, in general, I believe that radiation therapy will offer at least as good chances as surgery.

3. *The Rather Superficial Mucosal Carcinoma* that appears in the form of a flat, large ulceration which frequently, when recognized, does not encircle the entire lumen, is the least suitable type for surgery. The leading symptom is more commonly that of retrosternal pain due to secondary infection of the ulceration rather than obstruction. These tumors are particularly prone to early wide-spread lymphatic extension and distant spread. Very seldom, if ever, will such a tumor be curable when recognized, by either surgery or radiation therapy. It, therefore, is doubtful whether one is justified in subjecting a patient with this type of carcinoma to the greater discomfort associated with surgical removal. Because of the rapid progression of these tumors and their tendency to perforate through the esophageal wall together with the lack of obstructive symptoms, it may at times be preferable to withhold any therapy. Such patient is at times kept more comfortable by the use of antibiotics for treatment of the infection of the large ulceration.

The second important factor is the *location of the carcinoma in the particular segment of the esophagus.* Carcinomas of the cervical esophagus, for reasons previously discussed, are preferably treated by radiation therapy. In the presence of a lesion located in the thoracic portion, the higher surgical mortality in locations necessitating supra-aortic compared to infra-aortic anastomosis must be considered. In Sweet's series, the primary mortality following surgery for lesions in the lower fourth of the esophagus was 11.5 per cent (12:91) compared to 24.3 per cent (11:50) for lesions located in the mid-thoracic portion. Strieder and Lynch report in 58 low re-

sections performed since 1945 a primary mortality of 17.2 per cent compared with 30.7 per cent in 26 supra-aortic resections. Gibbon *et al.* report a primary surgical mortality of 10 per cent (3:29) following infra-aortic anastomosis as against 61 per cent (13:20) after supra-aortic anastomosis. Garlock, on the other hand, had a higher mortality in the infra-aortic than in the supra-aortic group (33 per cent and 24 per cent respectively).

Even if the primary mortality is disregarded and only those patients "who had an opportunity to survive" (Sweet)—this means who leave the hospital alive following resection—are considered, Sweet found after resection of the lower segment 17.4 per cent five year symptom freedom compared to only 4 per cent in the group of mid-thoracic lesions.

Thus, it would seem that the location in such a segment of the esophagus in which supra-aortic anastomosis would be necessary will in case of doubt rather weigh against surgery and for radiation therapy, while in lesions located in the lower segments, other things being equal, surgery should more seriously be considered.

The third factor which influences the decision is the patient's *age*. Sweet has shown that his primary mortality increases from 6 per cent in patients under forty-five years of age, to 25 per cent in patients over sixty-five years. In 43 postoperative deaths, pneumonia and septic complications represented only 7 instances, while cardiac failures and pulmonary embolism were the cause of postoperative death in 22 and 6 cases respectively. This would indicate that it is unlikely that, in patients of this age group, further marked improvement of primary mortality which is mainly due to cardiovascular complications can be expected. Considering also that of course the life expectancy decreases for other reasons with increasing age, it would thus seem that, other things being equal, radiotherapy should have increasing preference with increasing age.

SUMMARY AND CONCLUSIONS

1. In spite of improvement of surgical and radiological technical facilities during the last decade, the five year cure rate of patients with esophageal carcinoma to date remains extremely poor. Of all patients with carcinoma of the esophagus seen, not more than 2 or 3 per cent have survived five years.

2. If reasonably comparable material is compared, the statistical five year cure rate following surgery and radiation therapy is in the same range, namely around 3 per cent of all patients admitted for either exploration or irradiation, or around 3 to 6 per cent of patients "sufficiently" treated (resected or thoroughly irradiated).

3. A slight improvement of surgical and radiological results (due to reduced primary surgical mortality, improvement of technical facilities, increased technical skill and experience) is possible. Marked improvement in the over-all result is unlikely. The limitations of curability for the majority of cases are inherent in the biological character of the disease with its late recognition and its tendency to spread into the regional paraesophageal and mediastinal lymph nodes.

4. More careful selection of patients for resection has appreciably increased the relative cure rate: 12 per cent of all patients admitted for exploration and 28 per cent of all patients in whom resection could be done.

5. Palliative results as measured by symptom-free survival (with restoration of esophageal function) after one, two, and three years are the same following surgical resection with anastomosis or adequate roentgen therapy.

6. The conclusion appears justified that patients in whom the likelihood of surgical resection with permanent control is nil or unreasonably small may still receive equal palliation by adequate radiation therapy with considerably less morbidity inherent in the procedure.

7. Based on these considerations, an

outline of indications for better selection of patients for either surgery or radiation therapy is offered as a tentative suggestion. The main factors which determine such selection are the type of lesion, its location in the particular segment of the esophagus, and the patient's age.

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DISCUSSION

Dr. Jens Nielsen, Copenhagen, Denmark. I can show you the statistics of all cases of intrathoracic carcinoma of the esophagus and perhaps add a few words on the question of indications for surgical and radiation therapy in these tumors.

(Slide) We have surveyed 242 cases, all of of them inoperable, and as you see the results are practically the same as those Dr. Buschke showed. Of the total number we have about 2 per cent, 6 of 242, of what we call adequately treated cases which have had what would seem to be a sufficiently high tumor dose; not quite 5 per cent.

(Slide) If we look at the different locations in the esophagus, there would seem to be not much difference in the cases we have been able to make symptom-free with radiotherapy; it is nearly the same in the upper part of the esophagus as in the lower part.

(Slide) As Dr. Buschke said, the results are mostly palliative. We get a survival of up to 15 per cent of all the inoperable cases.

All our results so far have been palliative temporarily, but there is no doubt that this technique gives promise of delivering a sufficiently high localized tumor dose to the esophagus and its immediate surroundings without impairing too much the general and local condition of the patient. We have a rather large drop in our survival curve during the third year, and this seems to be due to metastases and local recurrences which show up even after three and four years, in some cases after five years; so that the five year salvage has been below 3 per cent.

Concerning the indications for surgical and roentgen therapy I think those can only be tentative and on broad lines at the present time. In favor of surgical treatment are the following factors; the better opportunity for judging the real state of the primary tumor, the metastasis, and for adequate action, especially locating and removing lymph node metastases if that is possible. Then, radioresistant adenocarcinomas, especially at the cardiac end of the esophagus, lend themselves—all other things being equal—quite as well as surgical excision as the more radiosensitive squamous cell carcinomas. Against operative treatment is the fact that resection of the esophagus is still a major procedure with a high operative mortality, especially in the superior part of the intrathoracic esophagus. Patients are mostly in the older age group and the diagnosis of carcinoma of the esophagus is, in the majority of cases, first made in the advanced stages because of the insidiousness of the disease. The conditions created by the operation in pulling the stomach into the thoracic cavity are not quite as radical or local continuity is obtained. On the side of the rotation treatment, I think, stands the fact that it is well tolerated by most patients, and it has been shown to be palliative in one-fourth of the patients for one year, and in nearly one-eighth of the patients for two years. Against rotational therapy is the fact that lymph node metastasis is probably ineffectively treated in cases where surgical extirpation might have effected a cure and this, in my opinion, is the weakest point in rotation therapy; also it does not give hope of cure in adenocarcinoma. And the actual five year survival figures are low. The treatment is time consuming and requires special technical facilities.

I feel that until a greater amount of material is at hand and until rotational irradiation with radioactive cobalt has been tried out, it would seem difficult to deny that surgical treatment of carcinoma of the esophagus offers the best theoretical possibilities of a cure of this disease, because it can deal more effectively with lymph node metastases. Even taking the higher operative mortality into account, it should be given preference, and rotation treatment should be reserved for inoperable cases. But I think that a careful discrimination between chances and risks should be made in each individual case on the background of the palliation offered by rotation therapy. I think that future results of rotation therapy with supervoltage roentgen therapy should be of special interest.

I might add that results in the cervical parts of the esophagus where the surgical technical difficulties are also rather high are not quite so disappointing as in the intrathoracic part. We have found that out of 108 cases of carcinoma of the cervical part of the esophagus we have been able to obtain five year freedom of symptoms in 9 cases—8 per cent. That is with 200 kv. and simple cross-firing technigue. So in this location it might be worth while to try roentgen therapy in a greater number of cases than in the intrathoracic part.

DR. WALTER L. STILSON, Los Angeles, Calif. This paper by Dr. Buschke is certainly very timely. In the Los Angeles area we do not get very much chance at these carcinomas of the esophagus. It has been our impression that our surgeons feel that they should resect and that irradiation does not have anything at all to offer in carcinoma of the esophagus, and I am therefore happy to hear Dr. Buschke's paper. That radiation therapy should not be given up in selected cases is illustrated by 3 cases we treated, in which ordinary 200 kv. therapy and radium tandem without the advantage of supervoltage has produced very good results, palliatively and histopathologically. One was a seventy-three year old female who survived for sixteen months and died of bronchopneumonia; at the time of postmortem there was no cancer at all. The second patient, a fifty-nine year old male, survived in healthy condition for two years and died suddenly,

with a coroner's diagnosis of heart attack. The third patient, a sixty-eight year old male, survived for nearly three years without recurrence. At the time of his death, no tumor was fond at autopsy. So I think we ought not to write off radiation therapy. I am very happy to hear this report by Dr. Buschke on the evaluation of radiation therapy as compared to surgery.

Dr. John L. Pool, New York, N. Y. As a surgeon it is very stimulating to hear this talk of Dr. Buschke's, and I must say that I agree thoroughly with his conclusions. I have one question I would like to ask him, but first I would like to re-emphasize and perhaps state slightly differently some of our experiences with this disease. I think the most difficult problem esophageal case is the patient who has a blocked esophagus—totally blocked—when he appears, and it is concerning that area that I would like to ask my question. I wonder what proportion of patients with a blocked esophagus have swallowing restored to the point that they are comfortable and not just on a thin liquid diet for the remaining eight to twelve months of life? We can tackle such problems either by radiation therapy primarily, by gastrostomy, or by attempted surgery and, in my opinion, in most of those patients, where there is no contraindication by reason of distant metastasis or general debility or secondary disease of some other sort, exploratory thoracotomy and attempted resection is the preferable procedure. I feel, as stated at this Society several years ago when Dr. Nielsen presented his figures, that if on exploration it is found that the cancer cannot be resected from the esophagus, at least the stomach can be brought up proximal to the obstructed area, and continuity for swallowing can be established by a so-called bypass operation. I think this leaves the patient in a more confortable condition than he would be with a gastrostomy.

As to the age group, and I perhaps could phrase this as a question to Dr. Buschke, I wonder if he feels that irradiation in patients past the age of seventy, with carcinoma of the esophagus, can be given with impunity; in other words, what is his feeling about the morbidity in this older age group? In my own experience in older people, thin older men in their seventies with a blocked esophagus, I think that surgery is preferable to irradiation. It is true that the mortality from operation is relatively high. In the last 70 consecutive resections we have had, our over-all mortality was 12 per cent; in those cases where the lesion was above the arch it was 20 per cent.

Finally, I am interested in Dr. Nielsen's remarks on the cervical esophagus, because certainly surgery in that area is mutilating, usually requiring removal of the larynx, and our surgical results have been nowhere nearly as good as those he presented for rotation radiation therapy.

Dr. Jens Nielsen, Copenhagen, Denmark (closing). I should say that almost all the older patients stand rotation therapy quite well. The only requirement is that the patient should be able to sit upright in a chair for the ten or fifteen minutes the treatment takes. The palliative results are, as we have found, quite satisfactory, so that many patients, I should say 40 or 50 per cent, are able to swallow not only fluids but also soft foods and some of them are able to eat naturally up to the time of death. Also, they died in a much more comfortable way. I think it is a question whether palliative surgery is preferable to rotational therapy in restoring continuity of the esophagus. That is one of the advantages we have found so far, in fact the only advantage, that it is tolerated so well by even older, dehydrated patients.

Concerning cervical cases, the reason we have so high a figure in cervical cases might be because of the female proportion of the material is rather high in Scandinavia because of the Plummer-Vinson syndrome, and we have found that the prognosis is considerably better in the female than in the male. We do have some cured cases in men, too, especially if the lesion is in a location which we think is typical for males. Generally, in our country, the involvement in the cervical part of the esophagus is mostly in women, but around the aortic arch, the preponderant proportion of the cases are in men. I should think that would be a difficult portion of the esophagus upon which to do a resection; even in this portion we have had the same results as higher in the esophagus.

Dr. Buschke (closing). I want to thank the discussants for their remarks, particularly Dr. Nielsen who has already answered most of the questions. With regard to Dr. Pool's questions:

We have not found that, in general, age itself in a well preserved body is an objection to radiation therapy—within reasonable limitations. This type of treatment is still, of course, a major procedure, and even for palliation, patients should be selected carefully, particularly from the point of general condition, loss of weight and degree of obstruction. How to handle a patient with complete obstruction I cannot answer in a few words. This depends on the individual situation. Occasionally we have felt that a temporary gastrostomy is indicated in order to make treatment possible. One of our patients who is now quite comfortable for two and a half years had a gastrostomy which was closed about one year after therapy. So far as the patient's support of treatment is concerned, this is usually tolerated well if patients are well selected and if they are treated under careful clinical supervision with adjustment of treatment to their tolerance. Poor tolerance has become much less of a problem since supervoltage is used.

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AN EVALUATION OF THE CLINICAL USE OF A STRONTIUM 90 BETA-RAY APPLICATOR WITH A REVIEW OF THE UNDERLYING PRINCIPLES*

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CLEVELAND, OHIO

THE strontium 90 beta-ray applicator for the eye was first reported by the present authors in 1950.[2,3] This applicator was developed to supplant the radon beta-ray applicator which was then in current use in our institution. As was pointed out in our original paper, Sr^{90} was selected because of its long half-life, energetic beta particles, and absence of gamma rays.*

At the time this applicator was being developed, it appeared to provide an excellent opportunity to establish dosage measurement in roentgen equivalent units which have already found acceptance for other forms of radiation utilized for biological purposes. Practically all previous biological studies employing beta rays unfortunately had no physical calibrations of the beta rays themselves. The dosages were generally recorded as the number of millicuries of radon, or milligrams of radium, applied for a specified period of time.[10] The common dosage unit was milligram or millicurie seconds. This merely indicates the number of disintegrations and very rarely reflects the dosage actually delivered in terms of energy transfer per gram of tissue (roentgen). It is well known to radiologists that exactly the same amount of radioactive element with differing filtration and geometric arrangement may give widely varying dosages.

In order to use the applicator effectively, certain underlying principles which are now established in radiation therapy were used for guidance.

a. A physical study of the emitted radiation, including depth dose measurements, was conducted.

b. A study of biological effects of this applicator as compared with other radiation on various tissues was made.

c. The clinical approach employed certain fundamental biological aspects of radiation therapy. These involved:

1. An attempt to fractionate the radiation dose so that the treatment would be delivered over a number of weeks.

2. An attempt to incorporate an assessment of the radiosensivity of the pathological process to be irradiated into the therapeutic plan.

As will be emphasized later, the use of fractionation and attention to the radiosensitivity of the lesion permits observation of the response to radiation during the course of treatment so that the dose may be matched with the biological response, thus utilizing the smallest possible dosage level for radiosensitive processes.

Although this report will concern itself primarily with the clinical effects and the radiation dosage schedules, it is important to point out that the principles outlined above were the basis for the decisions in treatment wherever possible. It appears desirable, therefore, to extend the discussion of these principles somewhat further.

* Sr^{90} decays to Y^{90}. Both are beta emitters without accompanying gamma rays. The energy of the Sr^{90} beta particle is 0.65 mev. and that from the Y^{90} is 2.32 mev. The half-life of Sr^{90} is 22 years. The value of an element having a long half-life cannot be emphasized too strongly. This means that the applicator does not require refabrication and replenishing at frequent intervals. In studying a number of radon applicators, we have found vast differences in the surface dose and in the depth dose curves. This is explained by the fact that the bulbs or tubes containing radon apparently cannot be duplicated exactly. Thus the gamma-ray emission is often useless in predicting the beta-ray dose (see Table II).

* From the Departments of Radiology and Surgery (Division of Ophthalmology), Western Reserve University and University Hospitals of Cleveland. Presented at the Thirty-fifth Annual Meeting, American Radium Society, St. Louis, Mo., April 20–22, 1953.

TABLE I
DEPTH DOSE TABLE

Depth (mm.)	Applicator					
	Ru^{106} (1)*	Sr^{90} (9)	Radon Burnam (3)	Radium (2)	Radon Hughes (2)	RaD+E (2)
0	100%	100%	100%	100%	100%	100%
1	55%	41%	31%	20%	8%	10%
2	30%	19%	13%	10%	2%	1%
3	17%	9%	6%	5%	1%	—
4	10%	4%	3%	2%	0.5%	—
5	6%	1%	1.5%	1%	0.3%	—

* Figures in parentheses indicate number of applicators measured. Depth doses shown are averages for all applicators measured.

PHYSICAL MEASUREMENTS

The present paper was prepared using data obtained from experience with two Sr^{90} applicators of significantly different construction.[5] The first of these was constructed at this institution and was used for about six months before being discarded because of leakage. It was unique in that it had an inherent filtration of about 100 mg/cm², a filtration which absorbed a large percentage (50 per cent) of the emitted beta particles. The second was a pilot model applicator* which was first used in October, 1949, and is still in use after more then three years. This latter applicator differs from the first mainly in inherent filtration, having a window thickness of only 20 mg/cm.[2] In addition to these two applicators, several other commercial models† were subjected to physical measurements and biological checks, but were not used clinically.

Initial physical measurements conducted upon the first applicator consisted of comparing film blackening in relation to the blackening produced by representative radon bulbs. All subsequent calibrations have been made using a specially designed extrapolation ionization chamber[6] which allows calibration in terms of the rep (roentgen equivalent physical), a unit which is directly related to the roentgen. The first applicator was calibrated only once with this ion chamber, but the second has been measured at frequent intervals since its first use. The surface dose values obtained for the latter applicator upon repeated calibration are in good agreement, having a spread of only ±5 per cent from the mean. The depth dose curve for this applicator has been unvarying and is nearly identical to the curve obtained for the first applicator which had a much higher inherent filtration. The depth dose curves of other commercial Sr^{90} applicators have been measured and shown essentially the same fall-off.*

Depth dose measurements for the Sr^{90} applicator and other applicators are shown in Table 1.

It should be noted that the depth dose for various applicators differs appreciably; Ru^{106} having the most energetic beta rays is by far the most penetrating, Ra D+E

* An experimental model supplied by Tracerlab, Incorporated, Boston, Mass.

† The commercial models measured were all Tracerlab applicators and were supplied by the following sources:

Ser. No. 179	Tracerlab, Inc.
Ser. No. 190	Tracerlab, Inc.
Ser. No. 1	Dr. Maurice Sachs, Veterans Administration Hospital, Cleveland.
Ser. No. 98	Dr. Harry Hauser, Cleveland City Hospital.
No Ser. No.	Dr. Otto Glasser, Cleveland Clinic.
Ser. No. 61	Dr. John D. Osmond, Cleveland, Ohio.
Ser. No. 29	Dr. J. A. Campbell, Indiana University, Indianapolis, Indiana.

* These applicators had intermediate filtration. The measurements, therefore, indicate that increased filtration does not affect depth dosage to an appreciable extent up to a depth of 5 mm. in tissue. The absorption curve for a single beta-ray spectrum is approximately exponential, that is, a straight line on semi-logarithmic paper. Radiation yielding such a curve cannot be hardened by increased filtration. The fact that such a situation exists for the Sr^{90}-Y^{90} applicator indicates that the weaker beta ray from Sr^{90} has been essentially eliminated by the inherent filtration, thus yielding a single beta-ray spectrum due to Y^{90}.

having the least energetic beta particles shows the greatest fall-off in depth.

It is also of interest to examine the surface dose emitted by applicators of the same type which have been replenished or refabricated at different times.

Table II shows the wide variations which were encountered.

TABLE II

SURFACE DOSE RATE

Applicator	Exposure mc. sec.	Surface Dose rep/sec.
Radon (Burnam)*		
I	100	51.2
II	100	14.9
III	100	4.04
Radon (Hughes)†		
I	100	413.0
II	100	290.0

* Prepared in our own radon plant.
† Procured from Radium Chemical Company.

Nonuniformity of the beta-ray dose in applicators of different types is due primarily to geometric considerations. The differences between individual applicators of the same type are due to the fact that the geometry and inherent filtration cannot be exactly duplicated. For highly penetrating radiation, this is generally of no concern. However, with beta rays this is critical since a few mg/sq. cm. will appreciably change the number of beta rays emitted. Generally, with radon applicators of different construction, the higher the surface dose, the greater the fall-off in the depth dose curve.

For the clinical use of any of these applicators, a full understanding of the depth dose is essential. Obviously, various levels of the cornea will receive different doses for the same surface irradiation, and for the same exposure, lesions deep in the cornea receive much smaller radiation doses than lesions close to the surface. In our experience, slit lamp examination has been invaluable in determining the depth of the process and, therefore, estimating the amount of radiation necessary for adequate treatment.

BIOLOGICAL CALIBRATION

In order to understand the biological effectiveness of the Sr^{90} beta-ray applicator, an attempt was made to calibrate the applicator on various tissues. The effect on the skin appealed to us immediately since this had previously been used for various types of ionizing radiation and the general characteristics of erythemas of the skin are fairly well known.

Skin erythemas were produced with various beta-ray applicators as well as with the roentgen ray (44 kv. Philips contact unit).[5] The beta-ray applicators which were included were Sr^{90}, Ra D+E and Ru^{106}.* These tests have shown that the skin reaction for equal radiation dose (as determined by independent means of calibration) using any of these sources is quite comparable. The energy of the beta particles from these sources differed considerably and the results would therefore suggest that differences in beta-ray energies in this general range had no effect on the biological reactions of the skin. It would indicate further that the extrapolation calibrations are valid and that dosages recorded in reps for the beta-ray applicator appear to approximate the dose in roentgens of a low voltage roentgen ray. Figure 1 shows the skin effects at various dosage levels. It is well to note that the erythema progresses with the increase in dosage and that the skin effects from the various applicators with similar doses are quite comparable. The skin treatments were given in single doses. During the first week, a mild reddening was noted which in many cases subsequently disappeared. The regular and more pronounced erythema appeared in twenty-five to thirty days. This does not readily fade, goes on to pigmentation, and at doses above 2,000 rep will show considerable and even marked desquamation.

Skin studies alone would not make it possible to predict the results of superficial

* We propose to use radon and radium applicators as well.

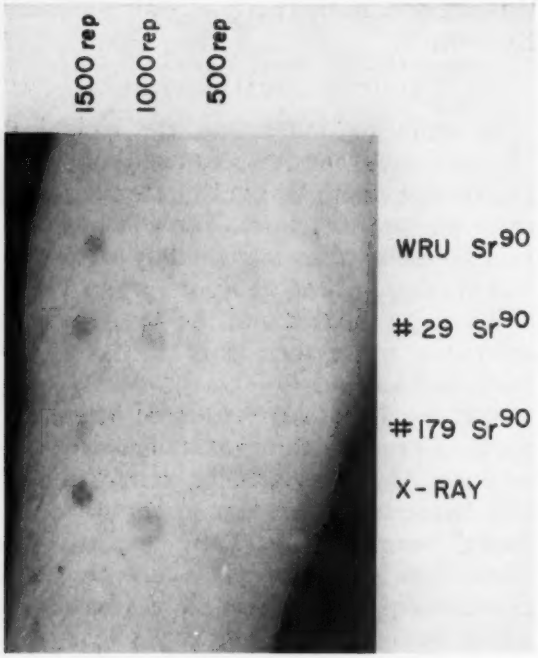

FIG. 1. Skin calibration of various Sr^{90} applicators with roentgen rays. The roentgen apparatus was a 44 kv. Philips, 3.8 cm. focal skin distance, no added filter. Sr^{90} applicator No. 179 proved on further study to have nonuniform distribution of the radioactive element, accounting for the less prominent skin reaction.

radiation of the normal or vascularized cornea. However, the skin studies help considerably in relating the beta radiation dosage used for various eye conditions to radiation dosage used in general therapeutic irradiation. Therefore, the effect on the normal cornea as well as vascularized corneas was also studied. Our experience with these tissues is much more limited. However, we were able to establish definite changes in the cornea after irradiation. The radiation effects on corneal tissues must be interpreted with great caution. Like all tissue that is avascular and high in collagen content, the stroma of the cornea is very resistant to radiation and can be exposed to extremely high doses without obvious evidence of injury. It is for this reason that the normal cornea appears unsatisfactory for evaluating the biological changes at comparatively low doses of radiation. The cornea will withstand high levels of radiation without injury and then at the highest doses, very abrupt changes with marked corneal effects will occur. F. M. Wilson[9] has shown that the minimal inflammatory reaction is noted only after exposure to 35,000 rep. We have made essentially the same observation. However, in all our studies, the epithelium showed radiation effects at considerably lower dosage levels, and the limbus, which often received comparable doses to the cornea, also showed marked cellular effect.*

Vascularized corneas were also studied. The data here are preliminary but the response to radiation appeared much earlier than in normal corneas. In this situation there was an extensive infiltration of fibroblasts and young vessels into the substance of the cornea, producing a general rearrangement of the stroma and a separation of the corneal fibrils. In vascularized areas, the vessels, after a comparatively short latent period, would suddenly break up with punctate extravasations of blood. The cornea would show no effects at this time, indicating that the vascular tissue was much more sensitive to radiation than the cornea proper. Our studies, both in humans and animals, lead us to believe that infiltrations of young fibroblasts and vascular buds are far more sensitive indicators of radiation effect. Unfortunately, this change is not easy to produce and to measure in experimental animals. It is our opinion that although excellent studies of both normal and vascularized cornea may be made, this structure is not responsive enough for biological calibration.

FUNDAMENTAL BIOLOGICAL ASPECTS OF THERAPEUTIC APPLICATION

As noted before, fractionation of the radiation dose is one of the cardinal tenets of

* We have initiated a study to determine the effect of high doses on human corneas. In a case in which the eye was to be removed for a tumor, 30,000 rep were administered in one dose directly to the cornea. Within one week there was evidence of epithelial injury, and three weeks later, when the eye was removed, there was extensive damage to the epithelium and stroma of the cornea. This is only a single example and therefore of uncertain significance, but it suggests that large doses may not be delivered with impunity.

general radiation therapy, and would appear to be useful in the treatment of eye lesions as well. Because of the problems of continually replenishing and refabricating our original radon source, fractionation was highly impractical and was not followed. The desire to fractionate the dose was one of the important reasons for the development of the Sr^{90} applicator.

In the treatment of our cases, one week was usually employed as a fractionation interval, but there is no evidence to indicate that this is an optimal one, and it may well prove that shorter periods between treatments are superior. As has been noted previously, fractionation permits one to assess the effectiveness of the irradiation and to terminate the treatment if the response is prompt, or to prolong and increase the treatment if the response is slow. This permits some individualization of each case and generally provides for the lowest effective dose.

The utilization of single doses requires that every lesion be treated at a level high enough to affect the more resistant, thereby over-irradiating unnecessarily in some instances.

It is particularly important in benign lesions to effect a satisfactory response with a minimum radiation dose since one should not risk a permanent radiation injury in these circumstances. Fractionated doses also permit the radiobiological differences between normal and abnormal tissues to become operative. Because of the difference in recovery rates, which are probably associated with faster growth and turnover of abnormal tissues, prolonged irradiation produces greater effect on the abnormal as compared with normal tissues.

The difference in the sensitivity of various pathological processes also deserves consideration. This, too, is one of the important principles of radiation therapy and an evaluation of the radiosensitivity of the process to be treated is extremely desirable. This will be discussed later. However, it may be stated that, on the whole, poorly differentiated, rapidly growing structures are more sensitive to ionizing radiation of all types, and newly formed vessels and young fibroblasts which appear in many corneal processes fall into such a category. Combining an estimate of the radiosensitivity of the corneal process and the fractionation of the radiation dose generally permits the smallest practicable dosage levels.

CLINICAL DATA

The method of treatment of corneal lesions has been described previously.[2,3] It consists simply of anesthetizing the eye with 1 per cent pontocaine, immobilizing the lids, and applying the applicator directly with full contact to the corneal process. In corneal disease, treatment is given along the limbus to affect the vessels near their origin. It is imperative that the center of the cornea be avoided whenever possible. Fractionation was practiced in every instance with the radiation given at weekly intervals. The output of our applicator was 30 rep per second, thus delivering 1,800 rep in sixty seconds.

In this institution, treatment of eye lesions has been a cooperative effort between the Departments of Ophthalmology and Radiology in an attempt to obtain the best evaluation of the treatment. The ophthalmologist is of the greatest assistance in the use of the slit lamp for estimation of the depth of the vascularization and the character of the vessels. In addition, the appearance of various eye lesions to the uninitiated is confusing and requires the careful attention of someone familiar with corneal disease.

In our original paper, we indicated that a number of lesions were treated successfully with comparatively small doses. We have found since then that in order to affect most of the processes, considerably larger amounts of beta radiation are necessary. When the applicator was first developed, a cautious clinical approach to treatment was made and surface lesions with newly formed vessels were selected for treatment. As intimated earlier, this

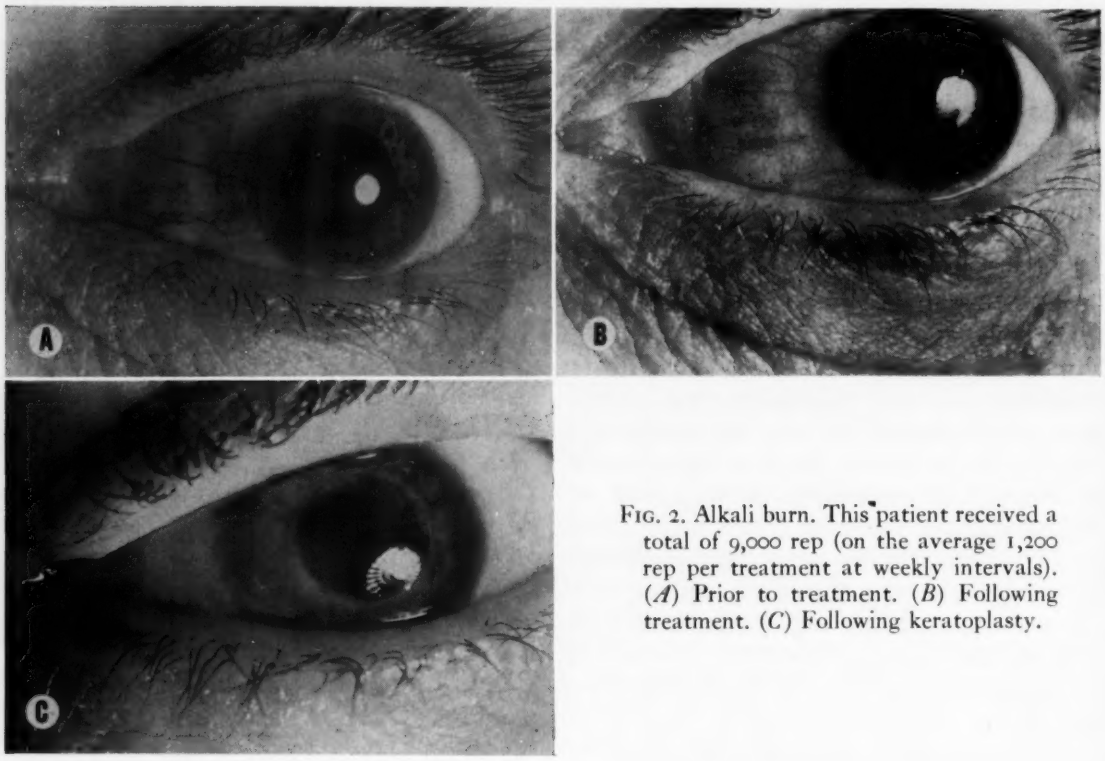

FIG. 2. Alkali burn. This patient received a total of 9,000 rep (on the average 1,200 rep per treatment at weekly intervals). (*A*) Prior to treatment. (*B*) Following treatment. (*C*) Following keratoplasty.

type of lesion is responsive to comparatively small doses.

In the following paragraphs is a description of the various conditions which have been treated, the response to treatment, and the dosage schedules we have used.

1. *Corneal Vascularization.* The beta-ray applicator found its primary use for obliteration of corneal vessels, and when successful, this application is probably of the greatest benefit.[7,8] Of our total of 137 cases, 65 were cases of corneal vascularization. Most of the cases have been vascularizations in individuals who were candidates for keratoplasty. In cases that are presented for keratoplasty, especially of the partially penetrating type, devascularization of the cornea is imperative for a successful result. Corneal vascularization may be considered generally under three categories: the superficial, deep, and mixed. The superficial type is generally encountered prior to keratoplasty, following keratoplasty and in corneal ulcerations.

In our series, 37 cases showed vascularization of the superficial type. As has been pointed out, when the vessels are superficial and newly formed, the response to beta irradiation is more satisfactory than in other types and the dosage depends upon the extent and depth of the corneal vascularization. This type of lesion was treated with varying dosages up to 12,000 rep, with the average dose in the order of 6,000 rep. The results, on the whole, were very satisfactory. As indicated in Table III, 24 of the 37 cases showed good response. In 6, the response was only moderate. We were unable to observe 7 of the patients and these are presumed to have had comparatively little beneficial effect. It is possible that if we had increased the dosage further, the response might have been even better. However, we hesitate to recommend higher doses. Figure 2 shows the kind of response to be observed following irradiation.

From our experience in these cases, we would recommend a dosage of 1,800 rep per treatment, at weekly intervals. We would hesitate to recommend a dose be-

TABLE III

SUMMARY OF ALL CASES TREATED OVER A PERIOD OF FIVE YEARS WITH THE Sr^{90} APPLICATOR

Diagnosis	No. of Cases	Dosage (rep)			Results*			
		Low	High	Average	o	+	++	+++
1. Vascularization								
a. Superficial	37	325	12,000	6,000	7	6	22	2
b. Deep	12	1,950	16,575	10,800	1	2	8	1
c. Mixed	16	2,975	21,500	10,800	0	4	11	1
2. Pterygium								
a. Beta radiation only	8	325	16,000	12,000	3	1	4	0
b. Surgery and postoperative beta radiation	12	1,300	14,800	4,000	0	0	8	4
3. Vernal Catarrh								
a. Palpebral	11	1,800	16,950	9,000	1	1	3	6
b. Limbal	4	3,250	9,600	6,000	0	0	2	2
4. Tumors								
a. Papilloma	11	450†	21,600	6,000	1	0	2	7
b. Hemangioma	3	1,320	3,000	3,400	0	2	1	0
c. Basal cell cancer of eyelid	1	3,900	—	—	0	0	0	1
d. Bowen's disease	1	1,950	—	—	0	0	1	0
e. Chalazion	5	650	5,300	2,600	0	0	5	0
5. Infection								
a. Tuberculous sclerokeratitis	5	1,800	7,375	5,400	0	0	0	5
b. Chronic conjunctivitis	1	17,800	—	—	0	0	1	0
c. Epidermic keratoconjunctivitis	1	2,400	—	—	1	0	0	0
d. Disciform keratitis	1	650	—	—	1	0	0	0
6. Miscellaneous								
b. Filamentary keratitis	3	1,950	2,275	2,000	3	0	0	0
b. Irritable scar	2	4,550	5,700	5,000	0	0	1	1
c. Epithelialization of anterior chamber	1	2,825	—	—	0	0	1	0
d. Epithelial dystrophy	1	650	—	—	1	0	0	0
e. Conjunctival cyst	1	5,200	—	—	0	1	0	0

* Results: o = no change; + = fair; ++ = good; +++ = excellent.
† Lesion disappeared with single small treatment.

yond 12,000 rep for superficial lesions and believe most of them will respond to approximately half this level.

Immediately following keratoplasty, reinvasion of blood vessels is often encountered. When this occurs, either in the vicinity of the graft or following superficial keratectomy, the new vessels are very radiosensitive and, as a result, the dosage need not be high. We recommend a dosage of 1,800 rep to be applied within forty-eight hours after operation, repeated every two to three days, with a maximum of 9,000 rep, and an average considerably lower.

Corneal ulcers of various kinds frequently show superficial vascularization and these ulcers often heal readily when the vessels are obliterated. Treatment should be applied to the limbus over the vascularized area.

Deep vascularization is found in interstitial keratitis of one kind or another, chiefly due to tuberculosis and syphilis. These cases often present themselves for

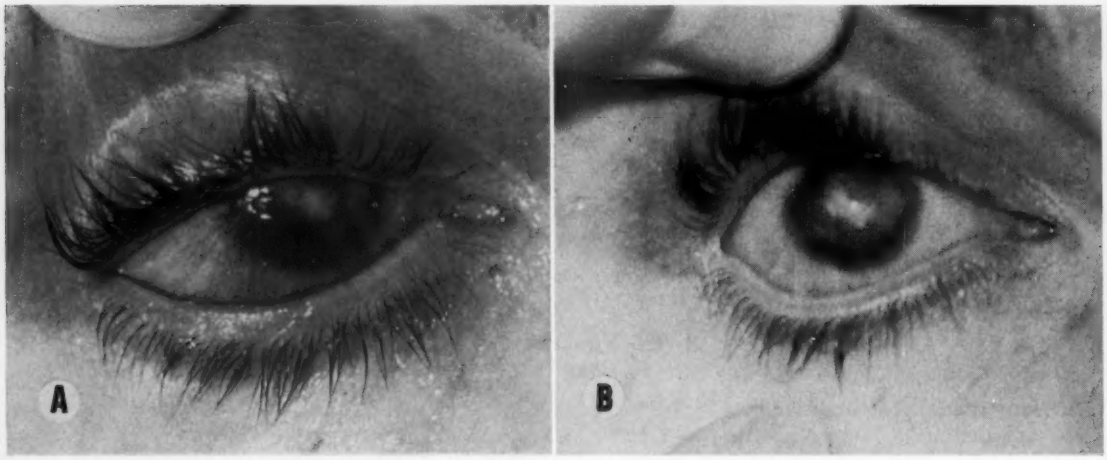

FIG. 3. Ammonia burn with extensive vascular infiltration. This patient received a total of 12,600 rep to each of three areas, 1,800 rep per treatment. Treatment was at varying intervals, some longer than one week, because his residence was at a great distance from the hospital. (*A*) Prior to treatment. (*B*) Following treatment.

keratoplasty and frequently vessels are present which must be obliterated. In general, such vascularization presents a difficult problem which requires higher dosages than the superficial type. In order to determine the progress being made during the course of their treatment, it is imperative to obtain slit lamp microscopy to evaluate the character of the vessels and the depth of the invasion. In our series of 12 cases, the dosage extended to approximately 17,000 rep, with an average of approximately 10,000 rep. All of these showed satisfactory results. It is to be noted that the dosage level is higher, which is in part explained by the fact that the process contains many old, deeply situated vessels.

With the mixed type of vascularization, the dosage would range from 3,000 to 21,000 rep. On the average, we delivered about 10,000 rep in a six-week interval. Figure 3 represents an example of the response.

2. *Pterygia.* This presents a condition which may be treated satisfactorily with beta radiation under most circumstances.[4,8] However, the type and thickness of the lesion here is of utmost importance. Bulky and well established pterygia with large vessels generally respond poorly unless very high doses are administered. Under such conditions, the best results were obtained when the pterygium was removed surgically and within forty-eight to seventy-two hours postoperatively irradiation was started. We treated a total of 20 cases, 8 of which were treated with radiation alone and the remainder by surgical removal and postoperative beta radiation. In the 8 cases treated by beta radiation alone, 5 showed satisfactory results, and 3 cases, in which the pterygia were of long standing and thick, we observed no effect. The dosages delivered here were, in general, considerably higher than for vascular lesions. They ranged up to 16,000 rep with an average of 12,000 rep. Figure 4 shows the effect of beta radiation on a long-standing but comparatively thin pterygium.

In the 12 cases which were treated by surgery and postoperative beta irradiation, the dosage was considerably lower. The average dose was approximately 4,000 rep, delivered at a rate of 600 rep per treatment. There was 1 case in which the dosage went to a total of approximately 15,000 rep. In these postoperative treatments, all of the results were very satisfactory.

In the light of our experience with pterygia, we would recommend the following: only thin, newly formed pterygia should be considered for beta radiation therapy initially. It is very likely that even the thickest

lesions, with well developed vessels, can be arrested with beta radiation, but the dosage required for these is unusually high and the risk of a radiation complication, we believe, becomes great. It would appear, therefore, that the thick lesions are best treated by removing the lesion and then instituting postoperative therapy to prevent recurrence which is the primary purpose of the treatment.

3. *Vernal Catarrh.* Satisfactory results were also obtained in the treatment of vernal catarrh by beta radiation. The fresh early cases responded best, whether of the limbal or palpebral type, and of these two varieties, the limbal requires less radiation than the palpebral. The follicles in vernal catarrh are very radiosensitive and will respond promptly to small doses of radiation. Unfortunately, they tend to recur and the dosage, therefore, for continued control, may go on to fairly high levels. Many of these lesions occur in children, and it is well, therefore, to treat with the smallest possible doses. We treated a total of 15 cases, 11 of the palpebral type and the remainder of the limbal variety.

The limbal lesions can be considered under acute and chronic varieties. The elevated gelatinous type that occurs at the limbus responds very well and levels off promptly with beta radiation. In our 4 cases, the dosage varied from 3,250 rep in the fresh type to 9,600 rep in the more chronic type. When the lesion has been present for a long period of time, or has become chronic due to frequent recurrences, fibrous tissue and granulations are produced which generally require higher dosages.

The response to radiation of the palpebral type is similar to that of the limbus, namely, better response in the acute lesions. In treating the palpebral type, special attention should be given to the follicles highest on the tarsal cartilage since these produce the most irritating symptoms. In our 11 cases, we delivered doses ranging from 1,800 to 16,000 rep. This large dose was delivered in two courses over a period of seven months. It is our opinion now, when dealing with a very chronic lesion which may require such a high dose, that the follicles be removed surgically and postoperative irradiation in much more modest doses be given. Figures 5 and 6 show regression of follicles following beta irradiation.

4. *Tumors.* Small papillomas of the eyelid are readily removed with the electric cautery or by means of excision, but some of these lesions are spread out along the lid margin and can be rather extensive. These latter appear to be treated best by irradia-

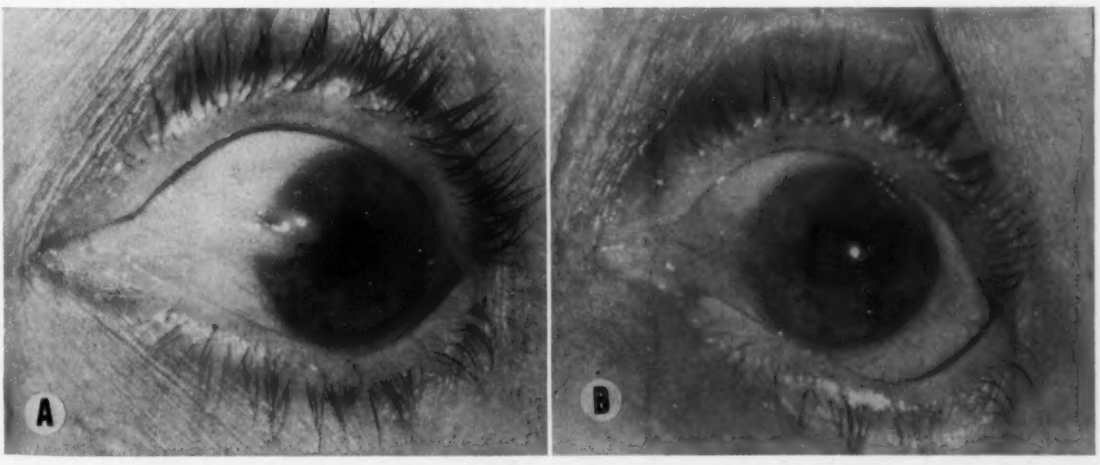

Fig. 4. Pterygium extending just over the limbus. This patient was treated with a total of 9,100 rep. He received 1,300 rep per treatment at weekly intervals. (*A*) Prior to treatment. (*B*) Following treatment.

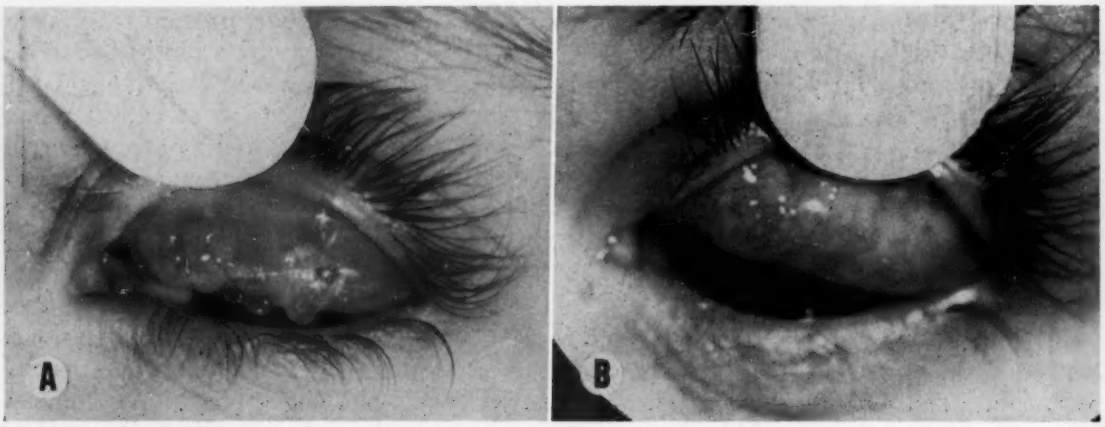

FIG. 5. Palpebral vernal catarrh. This patient was treated intermittently over a period of fifteen months. He received eight treatments of 1,800 rep each. (*A*) Prior to treatment. (*B*) Following treatment.

tion. When these lesions are located close to or on the lid border, there is frequently disappearance of the cilia with occasional permanent epilation. However, surgical excision of the tumor or cauterization also may result in a similar complication. The radiation dosage depends upon the depth of the lesion. In 8 cases the dosage ranged up to a total of 6,000 rep with very good results. We recommend single treatments of 1,200 rep, extending to a total of 6,000 rep.

Conjunctival papillomas also responded well to irradiation. Again, the required dosage varied in great measure with the depth of the lesion. The most frequent site of the tumor is in the limbus, and in this region the tumor has a decided tendency to recur. When excision is resorted to for their removal, postoperative irradiation is highly desirable to prevent the likelihood of recurrence. Three such tumors were treated with dosages ranging up to 16,800 rep. This unusually high dose was used in a large, thick papilloma and the treatment was given in two courses. In retrospect, surgical removal, with subsequent irradiation, might have been more desirable. Such high doses to the limbus predispose to glaucoma. This is due to an induced fibrosis in the region of Schlemm's canal or the destruction of the aqueous veins in this area. Figure 7 shows the regression observed following treatment of a conjunctival papilloma.

Our experience with papillomas of the

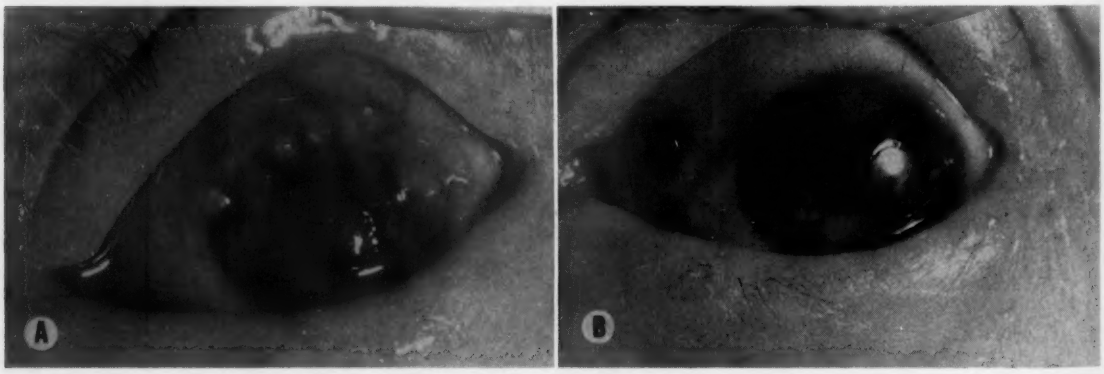

FIG. 6. Limbal vernal catarrh. This patient received a total of 3,900 rep given at the rate of 325 rep at weekly intervals. This was one of our early cases. We would now use larger doses to administer the treatment in a shorter period. (*A*) Prior to treatment. (*B*) Following treatment.

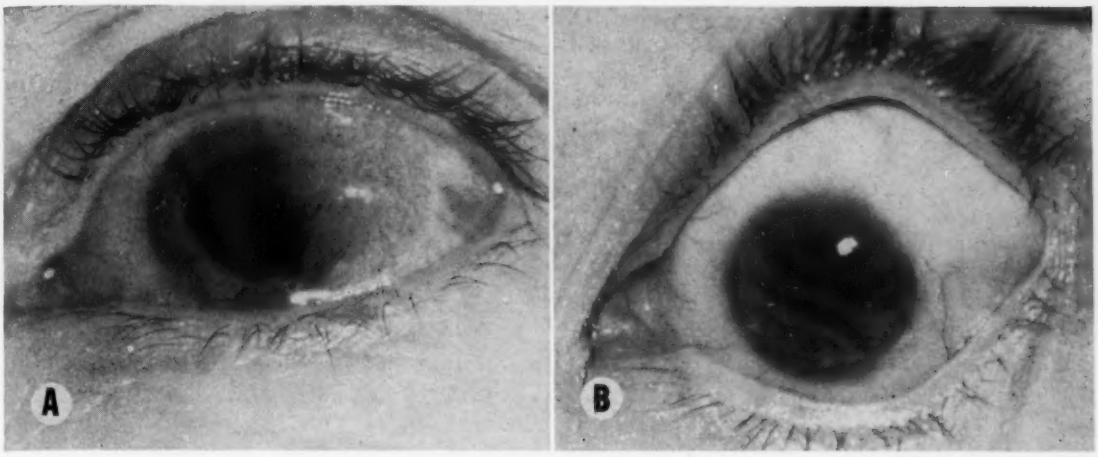

FIG. 7. Limbal papilloma. This patient received eight treatments of 1,800 rep each at weekly intervals. This lesion apparently was not covered completely by the applicator and a recurrence developed at one edge. This disappeared after additional treatment. (*A*) Prior to treatment. (*B*) Following treatment.

conjunctiva is rather limited and it is difficult to suggest a dosage schedule. They seem somewhat more resistant to therapy than those on the lid and it appears that the dosage per treatment should be somewhat higher. A dosage of 1,800 rep, repeated five or six times, should prove sufficient. It is important to remember that the treatment area of the bulb must cover the entire lesion. If the lesion is large, then several contiguous fields should be mapped out, with each area receiving the same dose.

Hemangiomas of the eyelid or conjunctival surfaces respond very well to radiation as do hemangiomas in other areas. These are found in infants and when small require comparatively little radiation to eradicate the process. We have treated 3 such cases with doses ranging from 1,300 to 3,000 rep in one or two treatments. After our experience with these, we would recommend 1,200 rep, given in single treatment, and perhaps repeated at monthly intervals once or twice, as indicated by the regression of the lesion. One should not be aggressive in treatment. Regression begins promptly but continues slowly.

The same principle can apply to epitheliomas either of the basal or squamous cell type. Here again, the accepted method of treatment is surgical removal followed by irradiation. One case of Bowen's disease was treated by beta radiation after the lesion had been excised. The area received 1,950 rep in two weekly treatments with satisfactory results.

One case of basal cell carcinoma of the eyelid was treated with beta radiation. This was a very superficial lesion which responded well to a total of 3,900 rep. We do not recommend treatment of basal cell carcinoma of the eyelid with beta-ray applicator. Superficial roentgen radiation, which is far more penetrating, is a much more effective method of treatment. Generally the eye can be readily shielded against this more penetrating radiation.

Five cases of chronic chalazion were treated in our series. Two of these were chronic inflammatory reactions occurring about a postoperative scar. We obtained satisfactory results in all of these instances. The doses here are considerably smaller, and 600 to 900 rep were given per treatment, with an average of 2,600 rep. Although these small doses appear effective, we recommend 1,200 rep, repeated two or three times.

5. *Infections.* In 5 cases of tuberculous sclerokeratitis, satisfactory results were obtained in all instances. Dosage ranged from 1,800 to 7,375 rep. In all of these cases, the applicator was placed directly on the site of inflammation. Figure 8 shows the

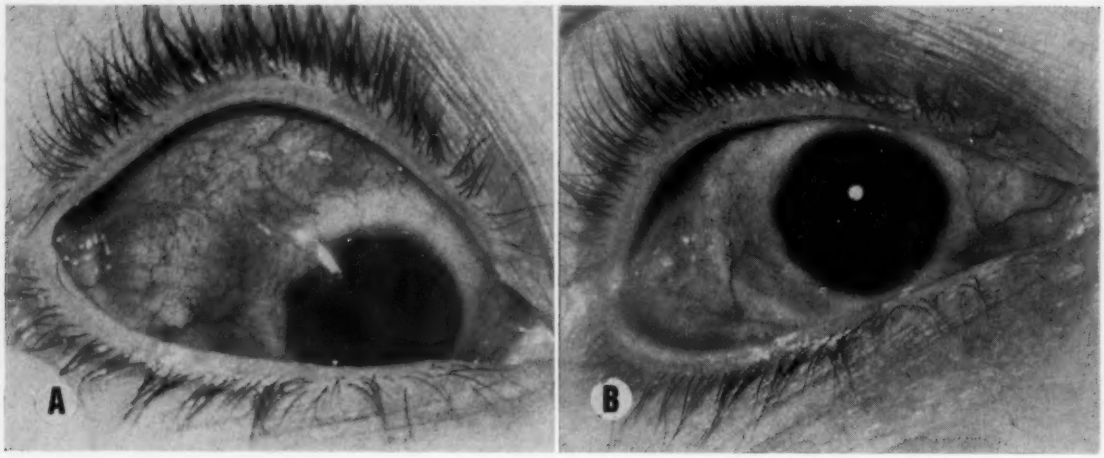

FIG. 8. Tuberculous sclerokeratitis. This patient received 5,400 rep to each of three fields, with 1,800 rep per treatment at weekly intervals. (*A*) Prior to treatment. (*B*) Following treatment.

response in a case of tuberculous sclerokeratitis.

One case of chronic conjunctivitis which had resisted all forms of therapy was treated with irradiation. This was of unknown etiology. The palpebral surface of the upper eyelid was thick, edematous and velvety in appearance with a moderate area of mucopurulent secretion. The patient received several courses over a period of fifteen months; 1,800 rep per treatment was given, with long intervals between treatments. The response was very satisfactory.

One case of epidemic keratoconjunctivitis and 1 case of disciform keratitis showed no effect from beta irradiation.

6. *Miscellaneous.* A number of miscellaneous conditions were treated to observe their effect. These are listed merely for information. Our experience in general has been so slight that we hesitate to offer any definite schedule for their treatment.

Three cases of filamentary keratitis were treated with dosages ranging from 1,950 rep to 2,275 rep without any change in the condition.

Two cases of irritable scar and associated cyclitis responded favorably to beta radiation with dosages from 4,550 to 5,700 rep.

One case of epithelization of the anterior chamber was arrested in its progress after the application of 2,825 rep to the advancing border.

One epithelial cyst of the conjunctiva was treated. These have a tendency to recur after incision. This cyst received 5,200 rep after drainage and did not recur.

DISCUSSION

When our first report was presented, it was intended at that time to bring to the fore the advantages of beta radiation arising from Sr^{90} as compared with other sources in current use. In that report we included a number of cases in which satisfactory results had been obtained with comparatively small doses—ranging up to 2,400 rep and given at the rate of about 325 rep per treatment at weekly intervals. It was never intended to establish a dosage schedule at that time, but unfortunately this dosage came into rather prevalent use. We have since found that this radiation dose was low except for very sensitive processes.

As noted in our clinical section, we have steadily increased our treatment and are now using radiation doses considerably higher than those originally reported. We still believe that the most satisfactory means of treatment is the use of divided doses at frequent intervals and this should prove superior to the single dose method.

As noted previously, the primary advantage is an opportunity to match the dose with the biological requirements, since the regression of the lesion may be observed during the course of treatment. It also permits the smallest practicable dose to be utilized.

Using some of the early, commercially prepared applicators, a number of other investigators encountered considerable difficulty. The difficulties appeared to be due primarily to the following causes:

1. Unsatisfactory calibration of the instrument. Many of the early applicators emitted considerably less radiation than their calibration indicated. This has since been corrected and the Tracerlab measurements correspond closely with our own.*

2. The general response to radiation for long-standing chronic processes is comparatively slow and often sufficient time was not permitted to elapse in order to observe the results.

3. Underlying the dosage problem is always the need for assessing the depth of the process, since the radiation falls off extremely rapidly from the surface.

4. Our original dosage schedule was probably insufficient for treating many lesions of the cornea.

As noted previously, our applicator produced an output of 30 rep per second at the surface. Since we used doses ranging from 600 to 2,400 rep per treatment, the application time was therefore in the order of twenty to eighty seconds. When the period of application is longer than one minute, difficulties in holding the applicator in position appear. It would therefore seem desirable to have somewhat greater beta-ray emission than is possible with our present applicator.†

In our experience, the optimum output would be 50 to 60 rep per second, so that the contact time is generally below one minute. With applicators having 100 rep per second output, it is obviously difficult to give a few hundred rep with any degree of accuracy since the time is so short. Also, the Bremstrahlen from this high output of beta rays becomes annoying and additional protection of personnel may be required.

The question of comparing the dose from beta rays, as reported in reps, with the dose in roentgens by conventional roentgen therapy, is still a problem for further study and evaluation. With superficial roentgen rays ranging up to 100 kv., there is very little change in the dosage over the first several millimeters, whereas with beta rays, arising from the Sr^{90} applicator, the dosage is reduced to 19 per cent of the surface dose after traversing 2 mm. of tissue. Generally, for various processes, 2,000 to 6,000 roentgens are delivered by conventional superficial roentgen rays to localized areas. This appears to be markedly different from the 12,000 to 20,000 rep that have been used in some eye lesions. However, if one would integrate the dose over the first 2 mm., a much closer approximation of the dose might be made. For example, the dosage over the first 2 mm. with superficial roentgen rays would still be close to 100 per cent of the surface dose, whereas integration over the first 2 mm. with the beta-ray applicator would represent about 50 per cent of the surface dose. Thus, 6,000 rep with a beta-ray applicator might be compared to 3,000 roentgens with conventional roentgen rays.

Some discussion of the radiosensitivity of the various types of lesions we have treated appears desirable. As indicated previously, one of the principles of radiation therapy is careful consideration of the radiosensitivity of the process to be treated. On the whole, poorly differentiated, rapidly growing structures are more sensitive to ionizing radiation of all types. In our experience, as well as that of others,[8] early, newly formed vessels and young fibroblasts, as well as hemangiomas of the cavernous type, were very sensitive to radiation.

Epithelial new growths, such as papillomas and the follicles of vernal catarrh,

* Numerous cross calibrations.

† It is our understanding that Tracerlab is now producing a variety of applicators, some of which have an output of 100 rep per second.

TABLE IV

SUMMARY OF DOSAGE SCHEDULE FOR BETA RADIATION

Type of Lesion	Dose per Treatment in Surface rep	Interval	Total Average Dose in Surface rep
VASCULARIZATION			
Superficial			
Prekeratoplasty	1,800	Weekly	7,200
Postkeratoplasty	1,200 or 1,800	2–3 days	4,800 to 6,000
Deep / Mixed	1,800	Weekly	10,800
PTERYGIA			
Preoperative (reserved for thin, flat, or early recurrence)	1,800	Weekly	12,000
Postoperative	600 to 1,200	Weekly	4,000 to 6,000
VERNAL CATARRH			
Limbal	1,200	Weekly	4,800 to 6,000
Palpebral	1,800	Bi-weekly*	9,000
TUMOR			
Papilloma			
Eyelid	1,200	Weekly	6,000
Conjunctiva	1,800	Weekly	7,200 to 9,000
Hemangioma	1,200	Monthly	3,600
Chalazion	1,200	Weekly	3,600
INFECTION			
Tuberculous sclerokeratitis	1,800	Weekly	5,400 to 7,200

* Monthly treatments may also be used.

also showed excellent response to comparatively modest doses, but were somewhat less sensitive than newly formed vascular tissue.

Least sensitive are well established pterygia that were thick and showed prominent well developed vessels. Certain types of interstitial keratitis with deep, well organized vessels also appeared very resistant to radiation.

In assessing the usefulness of the applicator, in our hands it has been of most value in controlling vascularization both prior to and following keratoplasty. Unless the vessels are controlled, the keratoplasty will not succeed. Following corneal transplantation, the newly formed vessels and fibroblasts which invade the cornea are effectively treated with comparatively small radiation doses and herein appears the most important application of the device.

The next most frequent use of the applicator has been in the case of pterygia and with this process the applicator has proved most successful when used postoperatively. Pterygia may be treated with beta rays alone, but this should be reserved for thin, comparatively new lesions. A long-standing, chronic, well established pterygium requires unusually high radiation dosages, and surgery plus beta radiation to prevent recurrences appears to be the method of choice.

New growths, such as papillomas, seem to respond exceptionally well to radiation, as does Bowen's disease. However, malignant lesions that are fairly thick, such as basal cell carcinoma of the eyelid, should not be treated with this applicator. Ordi-

nary radiation would appear to be preferable.

Vernal catarrh responds very well to irradiation and comparatively small doses are necessary. The applicator appears very useful in this condition and seems to control the follicles quite well. In long-standing chronic cases of vernal catarrh, or where the process is continually recurring, considerable attention should be paid to the mounting radiation dose which is often required. If the lesion does not respond to comparatively modest doses, other forms of therapy should be introduced.

We have observed no complications of any consequence with this applicator. The possibility of producing a cataract must always be kept in mind. We have estimated that the surface of the lens would receive less than 10 per cent of the dose delivered to the cornea. If one calculates the average dose given to the lens, assuming the lens to be 3 mm. in diameter, it proves to be approximately 3 per cent of that given to the corneal surface. The Sr^{90} applicator has been used for only four years and it is still possible that lenticular opacities might appear later. However, with our radon applicator which was previously in use for over ten years and which gave much larger doses to the lens, no evidence of cataract formation has been observed. It has been estimated that, for equal doses to the corneal surface, the radon applicator would deliver twice as much to the lens as the Sr^{90} source. This is due to the additional gamma rays from radon.

SUMMARY

The general principles of therapy utilizing beta rays from the Sr^{90} applicator for benign lesions of the eye have been reviewed. These include studies on the physical measurements of the beta-ray applicator, biological calibration, and basic tenets of the biological effects of radiation. The Sr^{90} applicator appears to be a useful source of radiation which has been effective in the control of various lesions of the eye.

A summary of 137 cases has been presented with an indication of the method of treatment, the response of the various types of corneal lesions, and the applied dose. A dosage schedule is included.

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RETICULUM CELL SARCOMA PRIMARY IN THE SKULL

REPORT OF THREE CASES

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GENERAL CONSIDERATIONS

VARIOUS terms have been applied to convey the pattern of histopathology found in this condition: lymphosarcoma, reticulosarcoma,[19] reticuloendothelioma,[8] retikelcellsarkom,[1] etc. When found in bone, most of these lesions have been considered metastatic from a reticulum cell sarcoma arising in lymph nodes or they have been diagnosed: endothelial myeloma, Hodgkin's disease, osteogenic sarcoma, clasmatocytic lymphoma, monocytoma, "inflammatory disease of bone" or "malignant disease of bone, unclassified."[8,12,20,21]

Ewing credits Kaufmann as being the first to recognize reticulum cell sarcoma primary in bone. In 1928, Oberling[16] postulated as to the potentialities of the reticulum cell, describing its possibilities of developing myeloid, lymphoid, plasmocytic, monocytic, or erythroblastic derivatives. His cytological scheme has served to reconcile the composite patterns not infrequently found with this neoplasm and to explain transitions (*i.e.*, as lymphosarcoma into lymphocytic leukemia, etc.). Following the publication of a series of 17 cases of primary reticulum cell sarcoma of bone, described by Parker and Jackson,[17] in 1939 Ewing[8] published a revision of the Classification of the Registry of Bone Sarcomas as compiled for the American College of Surgeons, identifying primary *reticulum cell sarcoma of bone* as an entity. However, relatively few cases have been so identified. In addition to Parker and Jackson's 17 cases, Sherman and Snyder[20] collected 17 cases. Coley, Higinbotham and Groesbeck[3] (including many of those described by Sherman and Snyder) have reported on 37 cases. McCormack, Ivins, Dahlin and Johnson[14] have reported on 25 "representative" cases. Otherwise Hatcher[9] reported 6 cases; Khanolkar,[10] 5 cases; Szutu and Hsieh,[22] 2 cases; Nielsen,[15] 2 cases; Ahlström,[1] Corbett[4] and Edwards,[7] each 1 case.

Craver and Copeland[5] provided an excellent study of lymphosarcoma. In their series of 164 cases, 10.4 per cent showed involvement of bone. Their compilation provides a comparison of the neoplasm primarily concerned with the lymph glands versus that primarily concerned with reticuloendothelial tissues in bone. Considering merely the over-all clinical aspects of these two apparently distinct neoplasms, the following generalities pertain (Table 1).

These criteria certainly are not clearly distinctive. The fact that reticulum cell sarcoma arising in lymph glands is prone to extend into adjacent bone and the fact that reticulum cell sarcoma arising in bone is prone to extend through the cortex, producing regional soft tissue tumefaction and regional involvement of lymph glands, has provided considerable consternation as to whether one or the other type of neoplasm has existed.[2,5,6,11,13,21] Too, oftentimes, the actual differential in these cases is dependent upon the clinical outcome.

ROENTGEN MANIFESTATIONS

The roentgen manifestations are helpful though they are not clear-cut.

Sites of Involvement. As above described, the tubular bones are most frequently involved (approximately 80 per cent of cases—half of which are located near the knee), in which case, the location usually is in the metaphyseal zone, with extension into the diaphysis or into the epiphysis, or

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Table I

	Reticulum Cell Sarcoma Arising in Lymph Glands	Reticulum Cell Sarcoma Primary in Bone
Age	Approximately 85 per cent of cases older than 40 years (less than 1 per cent under 20 years).	Approximately 75 per cent of cases less than 40 years (35 per cent less than 20 years)
Sex	1 to 2 males to 1 female	2 to 3 males to 1 female
Bone involvement	—In order of diminishing frequency—	
	Spine, pelvis, skull, femur, humerus, tibia, scapula, mandible, fibula, ribs	Femur, tibia, humerus, scapula, ilium, spine, fibula, clavicle
	Multiplicity of sites, the rule	Most cases identified as a single lesion; metastases to regional lymph glands, to the lungs or to other bones in untreated cases after a period of years
Rate of growth	Rapid; most cases dead within 5 to 8 months following bone involvement	Aggressive but likely continuing for months (*i.e.*, 4 to 48 months) before prompting medical attention; many cases surviving 7 to 18 years, following roentgen therapy
General systemic state of patient	Insidious toxic condition with progressive weakness, low grade fever, anemia and emaciation	General physical condition unchanged until very late; afebrile, little or no evidence of prostration
Predominant symptoms	Pain usually severe; unrelieved by rest; usually aggravating particularly at night. This pain is likely to be radicular in distribution and involving many levels. Complaints of "lumbago" are common	Pain, intermittent at first; of moderate or slight severity, usually localized; unrelieved by rest; likely to be referred to nearest joint; possibly abrupt onset of acute pain (pathological fracture)
Clinical findings	Multiple masses (adenopathy), weakness	Possibly diffuse tumefaction at site of lesion
Laboratory findings	Red blood cells and hemoglobin usually decreased; lymphocytes may be increased	Increased sedimentation rate

both. Flat bones such as the ilium, scapula or mandible may serve as the primary sites. Here, the involvement is usually more diffuse. Origin in the medullary portion of a diaphysis or in the cancellous structure appears to be the rule, with endosteal extension, primarily.

Mottling of osteolytic change; little or no osteoblastic reaction; lack of demarcation as to boundaries or involvement.

Possibly, fragmentation of bone cortex with the appearance of perpendicular striations (occasionally, there is vague lamellation of periosteal reaction or actual perpendicular periosteal striations); expansion of the cortex; pathological fractures not uncommon.

Parosteal soft tissue tumefaction characterized by large dimensions and indefinite margination; possibly, evidence of regional lymphadenopathy.

Possibly joint effusion—when lesion extends to proximity of joint.

Rapid response to roentgen therapy; spectacular involution of soft tissue tumefaction and early evidence of bone regeneration (reossifications noted as early as six weeks to three months following tissue doses as low as 1,700

–2,500 roentgens; "scar bone"—eventually, dense condensations at sites formerly occupied by tumor, characteristic.

HISTOPATHOLOGICAL CHARACTERISTICS

Even microscopically, this neoplasm is not too easily identified. However, the microscopic findings are the most tangible. The individual cells resemble those found in Ewing's endothelial myeloma, but in general there is a wider variation in the size and shape of the cell outlines. Usually, there are numerous large cells; their diameters varying from two to four times that of a lymphocyte. The nucleus of the reticulum cell is likely to be one and a half to three times greater than that of a lymphocyte. Binuclear cells are not uncommon but giant cells are rarely found. Not infrequently, the nucleus is indented or lobulated. The cytoplasm may be acidophilic or basophilic. Its volume is considerable as compared with that of the nucleus. Many of the larger cells show a reticular structure in the cytoplasm; an argentophil fibrillar network (particularly in the more slowly growing sections). This may be identifiable with hematoxylin and eosin staining or more definitely visualized by special reticulum staining (such as provided by the Gamori procedure). Reticulum fibrils characteristically surround individual cells or small groups of cells. The abundance of reticulum fibrils either as delicate strands or as dense bundles of collagen is especially featured in the case of reticulum cell sarcoma originating in bone. It has been theorized that it is because of the collagenous stroma and pseudocapsule that this neoplasm when primary in bone is slow growing. A not uncommon finding is invasion by cellular structure into veins or the development of infarctions with perivascular collections of lymphocytes.

In many sections, the masses of cells are of typical lymphocytes; in others, there are intermediary forms producing a composite pattern. Thus, with inadequate biopsy material, the picture may be so complicated as to lead to the erroneous diagnosis of an inflammatory process.

DIFFERENTIAL CONSIDERATIONS

Reticulum cell sarcoma primary in bone is likely to provoke consideration of several more common conditions:

Ewing's Endothelial Myeloma. The majority of patients afflicted with endothelial myeloma are in the second decade of life. The onset of this condition is similar to that found with reticulum cell sarcoma. Both conditions are featured by localized boring pain unrelieved by rest. However, with endothelial myeloma, a greater degree of systemic reaction is the rule; a low grade fever, likely leukocytosis and progressive anemia with emaciation. Roentgenographically, the lesions of endothelial myeloma initially are characterized by bone condensation, as a rule; later, by mottling of destruction as with primary reticulum cell sarcoma but even then lamellations of periosteal reaction and perpendicular striations of periosteal new bone formation are the rule. Regional soft tissue tumefaction of any appreciable degree is not usually featured in endothelial myeloma. Early metastases to the chest or to other bones is more characteristic of endothelial myeloma than with reticulum cell sarcoma primary in bone.

Primary Lymphosarcoma Arising in Soft Tissues with Metastasis to Bone. As above described, an immediate differentiation between this entity and reticulum cell sarcoma primary in bone is most difficult. However, particularly among the older age group, when prominent lymph nodes are featured, especially when there are multiple sites of bone involvement and the general systemic reaction is that of toxicity, fever and emaciation, certainly the guarded prognosis which pertains to lymphosarcoma primary in the soft tissues should be adopted. Though responsive to radiation therapy, this condition is multicentric to a degree that new sites of activity may be expected to become manifest from time to time.

Table II

	Parker and Jackson[17] (report on 4 cases of their own; 13 of the Registry of Bone Tumors)	Sherman and Snyder[20] (17 cases, Memorial Hospital)	Coley, Higinbotham and Groesbeck[3] (37 cases, Memorial Hospital, including most of Sherman and Snyder series)	McCormack, Ivins, Dahlin and Johnson[14] (report of 25 "representative" cases, obtained from files of Mayo Clinic)	Hatcher[9] (report of 6 cases, Univ. of Chicago)	Khanolkar[10]
Femur	5	4	8	9	2	1
Tibia	3	5	9	3	2	
Humerus	3	2	3	5		
Scapula	1	2	3	2		1
Ilium			4	3		
Clavicle	4				2	
Spine		2	2	1		
Fibula		1	2	1		
Rib		1	2			
Ulna			2	1		
Mandible	1					2
Sternum			2			1

Medullary Osetolytic Osteogenic Sarcoma. During the early phases of this condition, distinguishing characteristics may be lacking. Roentgenographically, the pattern of mere osteolytic mottling may duplicate that of reticulum cell sarcoma primary in bone. Evidence of striking perpendicular striations should prompt serious consideration of osteogenic sarcoma. Parosteal soft tissue tumefactions are common to both conditions though calcifications are more likely with osteogenic sarcoma. Histopathology should identify the latter. Furthermore, it is characterized by *lack* of response to roentgen therapy.

Osteolytic Metastasis. Metastatic lesions from a carcinoma of the breast, kidney or thyroid, in particular, may simulate the destruction in bone found with reticulum cell sarcoma. Breaks through the cortex with regional soft tissue tumefaction can be expected in any of these types of neoplasms. In most instances, where metastatic lesions are responsible, there are multiple sites of bone involvement and the primary lesion may be identified; otherwise, biopsy should serve to make the distinction. Response by metastatic lesions, such as considered, to radiation therapy is slower than that found with reticulum cell sarcoma primary in bone.

Hodgkin's Disease. This is usually featured by extensive adenopathy, enlarged liver and spleen and a general systemic toxic state. Histopathologically it should be distinguished by eosinophils and Reed-Sternberg cells.

Osteomyelitis. As with reticulum cell sarcoma primary in bone, osteomyelitis is prone to involve the metaphyseal zone in the beginning. Boring pain is characteristic. A regional soft tissue tumefaction is to be expected. However, with osteomyelitis, a febrile reaction is the rule, with associated leukocytosis. Biopsy should provide a distinctive histopathologic pattern; culture of the biopsy material should identify the infectious process.

Eosinophilic granuloma may be considered though it should readily be distinguished by virtue of the more uniform dissolution found in it; the substantial lamellation of periosteal reaction; the increased number of eosinophils in the blood stream and their conspicuous numbers scattered among large mononuclear histio-

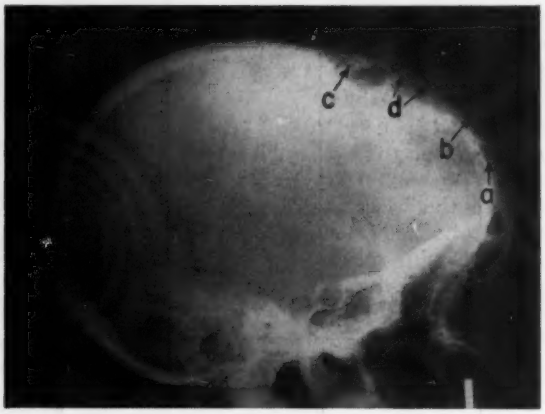

FIG. 1. Case 1. Lateral projection of the skull, February 4, 1946. As revealed stereoscopically, there was evidence of: (*a*) erosion of the outer aspect of the inner table with concavities outward; (*b*) dissolution of the outer table; (*c*) sequestrations, and (*d*) perpendicular striations extending into soft tissue tumefaction.

cytes in the biopsy material.

Reflex Hyperemic Deossification. The disseminated mottlings of deossification found in this condition simulate the pattern of osteolytic involvement found early in reticulum cell sarcoma primary in bone. Boring bone pain is featured in both conditions. With either condition, the temperature may be normal. Local swelling and edema may be featured with either condition though parosteal soft tissue tumefaction should distinguish reticulum cell sarcoma. Furthermore, details as to the history—background of basis for a nidus of irritability—should emphasize consideration of hyperemic deossification.

Though involvement of the skull is not uncommon as a metastatic lesion from reticulum cell sarcoma arising in soft tissues, search of the literature indicates that reticulum cell sarcoma primary in the skull is most unusual. Though several cases have been reported where indications were that the lesion was primary in the mandible, we have not been able to identify a single instance of this lesion arising in the cranial bones proper. Sherman and Snyder,[20] for instance, have stated: "We have no cases in the skull or small bones of the hands or feet." A glance at the incidence of locations in various parts of the body as reported by those having the largest series may be of interest (Table II).

CASE REPORTS

CASE 1. Mrs. M. C., aged fifty, was first seen by us (V.M.S), on February 4, 1946, at which time her complaints were of a swelling in the right frontal region. She had noted a small "lump" about six months prior to this visit; she described a very gradual increase in the size of it.

Because of the arrangement of her hair, the mass was not visible, though after retracting the hair and by palpation it seemed to be of dimensions approximating 6–8 cm. in greatest diameter with elevation superficial to the contour of the peripheral scalp to the extent of no more than 1–2 cm. The center of the mass felt somewhat doughy; the periphery, hard.

The general state of the patient appeared to be excellent. She was afebrile and showed no elevation of temperature regardless of repeated checking in the late afternoons and evenings. Her blood pressure varied from 170 systolic and diastolic to as much as 210 systolic and 120 diastolic. She described having had "hypertension for at least twenty years" to her knowledge, with frequent headaches.

Laboratory studies revealed no abnormalities; hemoglobin 82 per cent, 12.3 grams per 100 cc.; red blood cell count 4,380,000; white blood cell count 7,200, with 68 per cent polymorphonuclears, 4 per cent eosinophils, 20 per cent lymphocytes and 4 per cent monocytes. Repeated serological examinations indicated negative Kolmer and Kahn reactions. Urine examinations were essentially negative.

Roentgenograms taken on February 4, 1946 (Fig. 1), revealed dissolution of the outer aspect of the innter table; expansion and dissolution of the outer table with sequestration and obvious strands of ossification extending into a superficial soft tissue tumefaction.

Following an interval of consultation, a biopsy was taken on April 5, 1946. The histopathology (Fig. 2) was reported as reticulum cell lymphosarcoma with description as follows: "Sections show a tumor composed of loosely arranged basophilic cells of the lymphocytic series. The cells are supported by a very delicate reticulum with a sinusoidal architecture. There are numerous mitotic figures as well as scat-

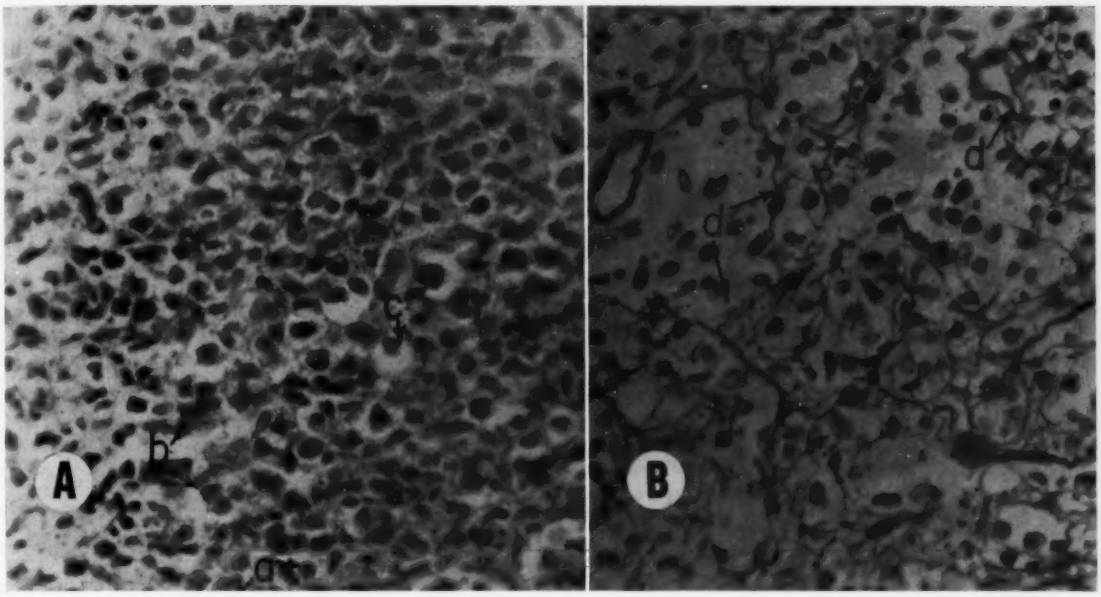

Fig. 2. Case 1. Biopsy* April 5, 1946. (*A*) Hematoxylin and eosin stain. (*B*) Silver reticulum stain. Observe: (*a*) lymphocytes; (*b*) pleomorphic and polyhedral reticulocytes; (*c*) histiocytes, and (*d*) reticulum strands extending from cytoplasmic poles of reticulocytes visualized by silver stain.

tered small areas of cellular disintegration and necrosis. Silver reticulum stains reveal an abundance of delicate reticulum intimately associated with the tumor cells."

Roentgen therapy was begun on April 16, 1946. Treatments were given daily (except Sunday) from that date to and including May 3, 1946. The radiation was applied through three portals: anterior frontal (roughly 7 cm. square), 1,600 roentgens (as measured in air); right and left oblique frontals, each 7 cm. square, 600 r (as measured in air). The radiation was of quality such as produced with a kilovoltage of 200; filtration added to a half-value layer of 0.8 mm. Cu. It is estimated that the minimal tumor dose approximated 1,000 r.

Interval re-examinations have been accomplished every six months. As shown in Figure 3, seven years following the onset of treatments, there has been complete involution of the tumefaction and restitution of new bone with "scar bone" in the area formerly involved by neoplastic destruction.

This patient has remained well, except for her hypertension during this period of time though a very small nodule developed at the base of her nose in April, 1951. Histopathology revealed findings similar to those of the original lesion. This lesion received treatment in the amount of 1,700 r. during the period April 13-May 3, 1950. There has been no evidence of recurrence at this site nor elsewhere. The area treated was 3 cm. in diameter. The radiation was of quality such as produced with a kilovoltage of 140; filtration added to a half-value layer of 1.9 mm. Al.

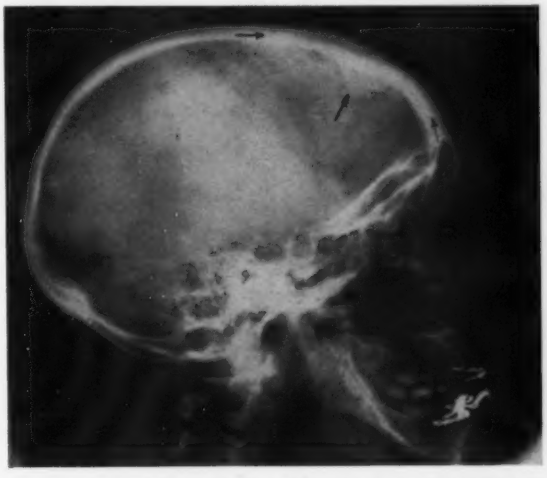

Fig. 3. Case 1. Re-examination seven years following treatment. Observe the dense sclerotic bone repair —"scar bone" (arrows).

* We are indebted to Dr. Joseph L. Zundell and Dr. G. Hal De May, pathologists, St. Francis Memorial Hospital, for their suggestion of pertinent fields, their accomplishing microphotography and identifying diagnostic criteria for these reproductions.

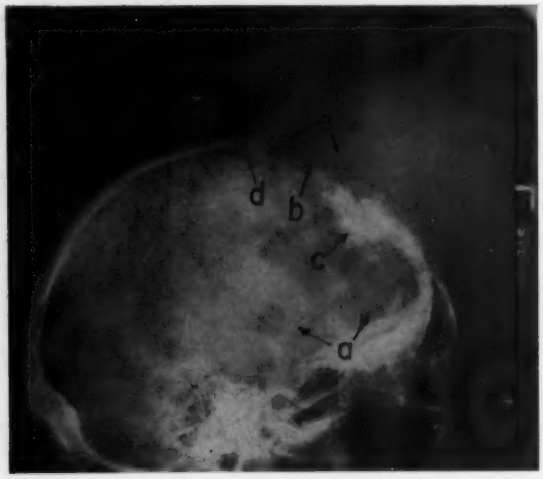

FIG. 4. Case II. Lateral skull projection. Observe: (*a*) diffuse mottling of deossification; (*b*) dissolution of the outer table; (*c*) sequestration; (*d*) evidence of erosion of the outer aspect of the inner table with concavity directed outwardly; (*e*) perpendicular striations and mottlings of calcification extending into large soft tissue tumefaction.

six or eight months prior to that time; she had been told by her hair dresser that they were due to large oil glands. During the two months prior to her coming in, these "bumps" grew together and enlarged considerably. She denied having had any pain at any time, though she had noted some loss of smell and taste, tingling in her fingers and toes and she described extreme apprehension and nervousness associated with menopause manifest during the previous six months.

The size of the mass can be appreciated by roentgenograms (Fig. 4) taken at that time. This mass felt doughy. It was nontender.

The patient was afebrile and showed no evidence of toxicity. Her blood pressure was 110 systolic, 65 diastolic. The hemoglobin was 80 per cent (12 grams per 100 cc.); red blood cells 4,240,000; white blood cells 5,100, of which 63 per cent were polymorphonuclears, 2 per cent eosinophils, 28 per cent lymphocytes and 7 per cent large mononuclears.

Biopsy taken on February 18, 1952, was reported as reticulum cell sarcoma. The following notation was made: "Sections show a highly cellular tumor composed of pleomorphic and hyperchromatic cells, many of which are in mitosis. No pattern of architectural arrangement is present. The cells in general are relatively large and silver reticulum stains show reticulum fibrils extending from and being de-

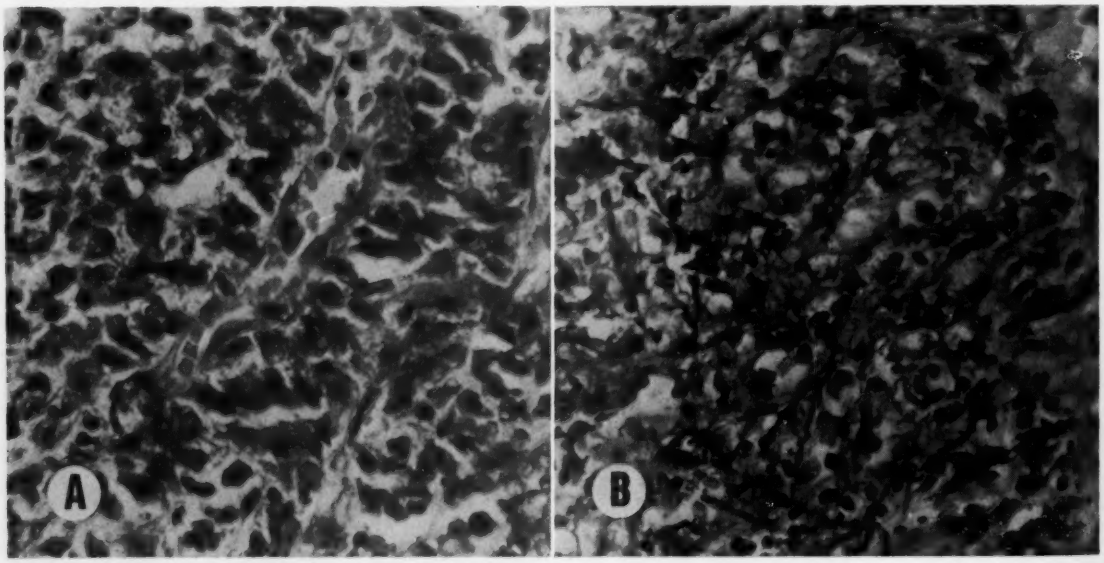

FIG. 5. Case II. Biopsy* February 18, 1952. Note the compact collections of pleomorphic and polyhedral cells and histiocytes as visualized by hematoxylin and eosin stain (*A*), and the diffuse sheets of reticulum revealed by the silver stain (*B*). Compare with pattern found in Case I (Fig. 2).

CASE II. Mrs. C. A. aged forty-seven, sought medical attention on February 15, 1952, because of a "lump on her head." She stated that she had noted three small "bumps" in the area

* We are indebted to Dr. Joseph L. Zundell and Dr. G. Hal De May, pathologists, St. Francis Memorial Hospital, for their suggestion of pertinent fields, their accomplishing microphotography and identifying diagnostic criteria for these reproductions.

veloped by the tumor cells. These are in the form of cytoplasmic fibrils in some cells, while in others a thread of reticulum extends from one pole of the cell" (Fig. 5).

Roentgen therapy was started on February 19, 1952; treatments were given daily (except Sunday) from that date through and including March 19. The radiation was applied through four portals: an occipital portal 10 by 15 cm. receiving 600 r (as measured in air); a frontal portal, 10 by 15 cm. receiving 600 r (as measured in air); right lateral portal and left lateral portal, each 10 by 10 cm. and each receiving 1,000 r (as measured in air). The radiation was of a quality such as produced with a kilovoltage of 250; filtration added to a half-value layer of 2.78 mm. Cu. The daily treatments were limited to 100 r (as measured in air) delivered to each of two portals. With consideration of maximum depth from each surface, it is calculated that the minimal tumor dose amounted to 1,800 r; the maximum tumor dose 2,200 r.

Interval re-examinations revealed progressive involution of the soft tissue tumefaction. When seen on April 4, 1952, there was no residual prominence of it whatsoever. The skin was smooth and there was complete depilation extending posteriorly to below the lambda. When seen on September 22, 1952, she showed excellent re-growth of hair. Roentgenography revealed deossifications or residual mottlings of dissolution of the external table. One year following the conclusion of the roentgen treatments (Fig. 6), there was evidence of substantial reossification.

Fig. 6. Case II. Lateral projection of skull, March 24, 1952. Observe the restoration of the outer table and the "scar bone" (arrows) obliterating the diploetic space.

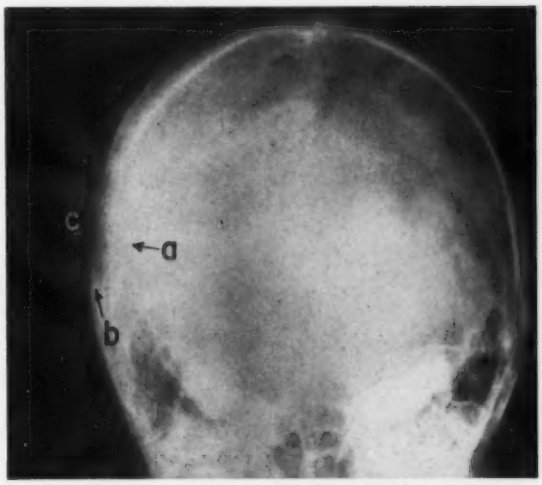

Fig. 7. Case III. Fronto-occipital projection of skull, March 12, 1952. Observe: (*a*) mottlings of bone destruction; (*b*) evidence of erosion of the outer table, minimal destruction of the outer aspect of the inner table, and (*c*) soft tissue tumefaction with no evidence of perpendicular striation nor of osseous debris.

Case III. Mrs. J. H. M., aged sixty-six, consulted her physician* on March 12, 1952, because of a "lump" on the right side of her head which she had first noted some eight months previously. She stated that it had gradually enlarged during that interval of time. About five months prior to this visit she had noted that the vision in her right eye was deficient and she had consulted an "eye specialist" who told her that "glasses would not help," but that she should consult her physician. During the same period of time she had suffered pain in her left shoulder.

Her general physical condition appeared excellent. She was afebrile and nontoxic. The mass on her skull was of prominence to the extent of about 6 cm. in diameter extending from the external aspect of the right parietal and including the squamosal portion of the right temporal, with elevation to a maximum of about 1.5 cm. The mass was nontender and hard. A somewhat tender lymph node was palpated in the right preauricular region, this being no larger than 1 cm. in diameter.

Retinoscopic studies revealed pigmentation

* This patient was referred to us for treatment by Dr. Francis J. Stanghellini who kindly provided the clinical details.

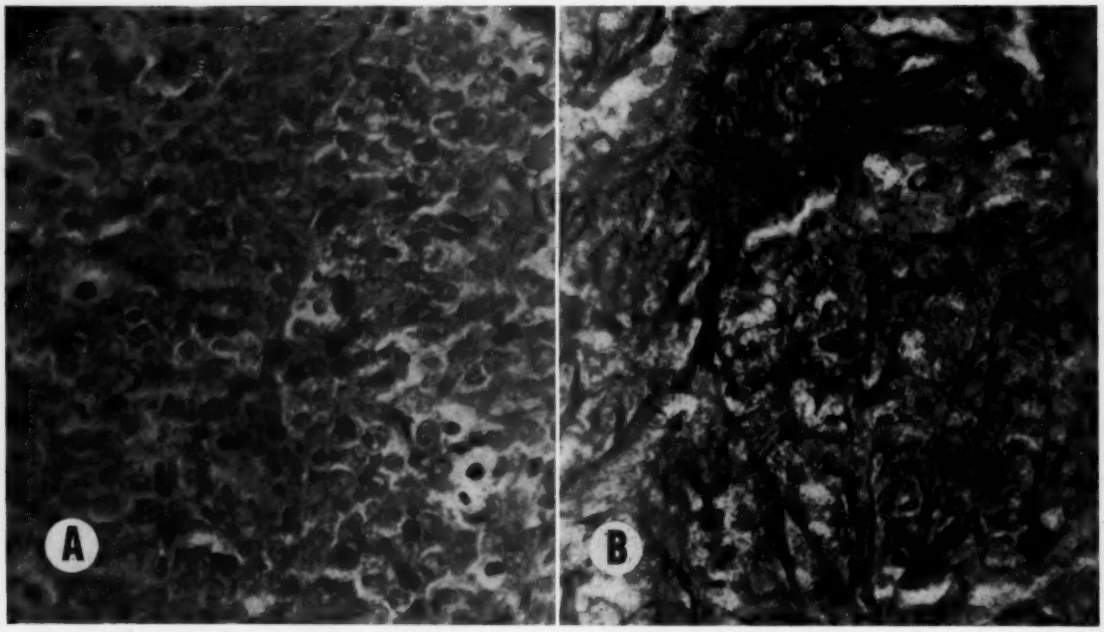

FIG. 8. Case III. Biopsy July 1, 1952. Whereas roentgenography indicated a fast growing lesion in this case, observe that the cell pattern is practically identical with that found in Case I (Fig. 2) and Case II (Fig. 5), unless one might consider a more compact cellular structure here; the sheets of reticulum are comparably compact. (See footnote, page 46.)

and fibrosis in the retina with gross hemorrhage in the vitreous.

A biopsy was obtained on July 1, 1952; the diagnosis reported was reticulum cell sarcoma. The following notation was made: "Sections through the nodule of subcutaneous connective tissue reveal an extensive infiltration by lymphoma of reticulum cell type. The cells are moderately large and on special stain reveal a basket-like network of reticulum fibers infiltrating the tumor. Abnormal mitoses are present and there is a moderate variation in the nuclei with some areas showing degenerative changes."

Roentgen therapy was started on July 3, 1952; treatments were given daily (except Sunday) from that date to and including July 17. The treatment portal was 10 by 12 cm., including the upper half of the parotid, the lateral portion of the right parietal, the entire right temporal and the anterior portion of the right occipital. The pinna of the ear was folded down and protected with lead. A summation dosage of 2,000 r (as measured in air) was delivered during this interval of time; the first four treatments being limited to 100 r (as measured in air); the remainder at the rate of 200 r each time. The radiation was of a quality such as produced with a kilovoltage of 250; filtration added to a half-value layer of 2.78 mm. Cu. It was thus calculated that the depth dose at 1 cm. amounted to 2,400 r.

When seen on July 28, 1952, there still remained a considerable mass in the central portions where formerly the maximum depth had been noted. Accordingly, additional treatment was given over a portal 8 by 10 cm., providing additional dosage in the amount of 600 r (as measured in air). This latter radiation was of a quality such as produced with a kilovoltage of 250; filtration added to a half-value layer of 1.53 mm. Cu. With the added dosage it was calculated that at a tumor depth of 1 cm. the summation dosage (including the first series) amounted to 2,900 r.

Re-examinations were made at intervals of one month. On August 12, there was practically complete depilation over the right side of the head; no residual tumefaction.

When seen on January 5, 1953, two slightly enlarged lymph nodes were palpated in the superior aspect of the right cervical triangle. These, too, were slightly tender. Accordingly, encompassing a 4 cm. portal, radiation was provided to a summation dosage of 2,800 r (measured in air); treatments were given at the rate

Fig. 9. Case III. Fronto-occipital projection of skull,* March 23, 1953. Observe: (*a*) restoration of outer table; no evidence of overlying soft tissue tumefaction; (*b*) sclerosis of inner table and diploetic structures—"scar bone."

of 400 r each day during the period of January 5–10, 1953. This radiation was of quality such as produced with a kilovoltage of 140; filtration added to a half-value layer of 2.9 mm. Al. It was calculated that the depth dose at 1 cm. amounted to approximately 2,600 r.

DISCUSSION

These 3 cases of reticulum cell sarcoma in the skull are presented as lesions apparently primary in bone. Cases I and II showed roentgenographic features typical of those reported by others, in cases of lesions located mainly in the long bones (otherwise in the scapula, ilium or spine). These 2 cases showed evidence of erosion of the outer aspect of the inner table with outward concavity; dissolution of the outer table—indication of origin in the diploetic cancellous structure.[18] They showed sequestration, perhaps due to tumor infarctions as described histopathologically, and they both showed perpendicular striations —indicating infiltration of neoplasm through porous channels in the outer table with apparent fibro-osteoid reaction of the epicranium. They responded promptly to relatively low tumor dosage: 1,000 roentgens in the one case, with no evidence of recurrence locally over a period of more than seven years; the calculated minimal tumor dosage of 1,800 roentgens in the second case, with no evidence of recurrence after one year. Roentgenographically, both cases showed healing by way of a dense sclerotic bone—the "scar bone."

The third case differed somewhat. Roentgenography indicated dissolution of the outer table; evidence of very little erosion of the outer aspect of the inner table. There was no evidence of perpendicular striation in the soft tissue tumefaction. Apparently this was a faster growing neoplasm. When first seen, there was evidence of extension into regional lymph nodes adjacent to the parotid gland.

With reference to the observations recorded in the literature, it is anticipated that our Case III is the most likely to show metastatic activities. Unlike the evidence noted in Cases I and II, there seemed here to be a lack of histopathological restraint. A limited longevity is anticipated for our Case III.

Though reports by others indicate that males are involved by this type of lesion more frequently than females and that most cases are of the age group less than forty years, all 3 of our patients were females, their ages being forty-eight, fifty and sixty-six years.

SUMMARY

A brief review of the literature is presented on reticulum cell sarcoma primary in bone. In particular, this lesion has been compared with reticulum cell sarcoma aris-

* Re-examination on November 8, 1953, showed no evidence of local recurrence.

ing in soft tissues and metastatic to bone. Apparently there have been no cases previously reported where this lesion developed primarily in the skull. Three such cases are presented here.

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Vol. 71, No. 1

ANOMALIES OF THE BONY ORBIT

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DEFECTS in the bones forming the orbit may be congenital or acquired. In the medical literature the congenital type has been described under three headings: orbital meningocele, osseous manifestations of neurofibromatosis and congenital absence of a portion of the bony orbit, depending upon the particular aspect of this condition that has been most impressive to the observer. LeWald[9] and Robertson[16] stressed the absence of portions of the bony orbit and called it a congenital absence of the superior orbital wall or a developmental defect of the sphenoid bone. Dandy[5] and Strandberg[20] termed the condition orbital meningocele while others[12,13,14,17,18] have been more impressed with the associated neurofibromatosis and have assumed a causal relationship between them. It is likely that all of these represent different aspects of a single entity with variable clinical manifestations.

Although this condition is quite rare, its recognition is of some practical importance since experience in the past indicates that this anomaly may be misinterpreted as bone destruction and a diagnosis of malignancy entertained. This occurred in a case described by LeWald[9] and in a similar example reported by Rockliffe and Parsons[17] where removal of the orbital contents was done because of an erroneous diagnosis of sarcoma of the orbit, and was followed by death of the patient. A patient described by Peyton and Simmons[13] was given a course of roentgen therapy on the assumption that the underlying condition was a retrobulbar tumor. In one of our cases the diagnosis of a neoplasm was seriously considered. Because of the significance and rarity of this condition we felt that it would be of value to report our experiences and to emphasize the roentgen characteristics by which the lesions may be readily recognized.

Case 1. W. E. W. The parents of this eleven month old male infant sought medical advice because of a mass in the left temporal region. When the infant was three months old, the mother had first noted masses in both temporal areas about the size of a marble but the mass on the right side gradually disappeared while the one on the left not only persisted but increased in size. She also observed that the mass bulged whenever the infant cried and that he could not close his left eye as well as the right eye. This was especially noticeable during sleep. For the past three months the mother stated that there was a definite prominence of the left eye associated with a serous discharge. Development was otherwise normal. There were two siblings who were completely normal.

Examination of the child disclosed an asymmetrical head with a prominence in the left temporal region and slight proptosis of the left eye. On palpation of the left temporal area it felt soft and cystic. Deep to the mass one could feel a diamond-shaped bony defect with edges that flared out and that measured approximately 2 by 3 cm. The mass seemed to be filled with fluid that pulsated synchronously with the heart beat and bulged whenever the infant cried. The remainder of the physical as well as the neurological examination was negative.

Roentgen examination of the skull revealed a symmetrical cranium except for a convex bulge in the left temporal region (Fig. 1). At the apex of this bulge the bony wall was absent. The bony structure of the right orbit was normal, but in the left orbit the usual bony landmarks, such as the optic foramen, lesser wing of the sphenoid and superior orbital fissure were not present. This was apparently due to the complete absence of the left half of the spenoid bone. In the lateral projection (Fig. 3) an ill-defined area of bone defect could be discerned in the region usually occupied by the greater wing of the sphenoid. In the Towne projection (Fig. 2), the osseous hiatus in the temporal region could be

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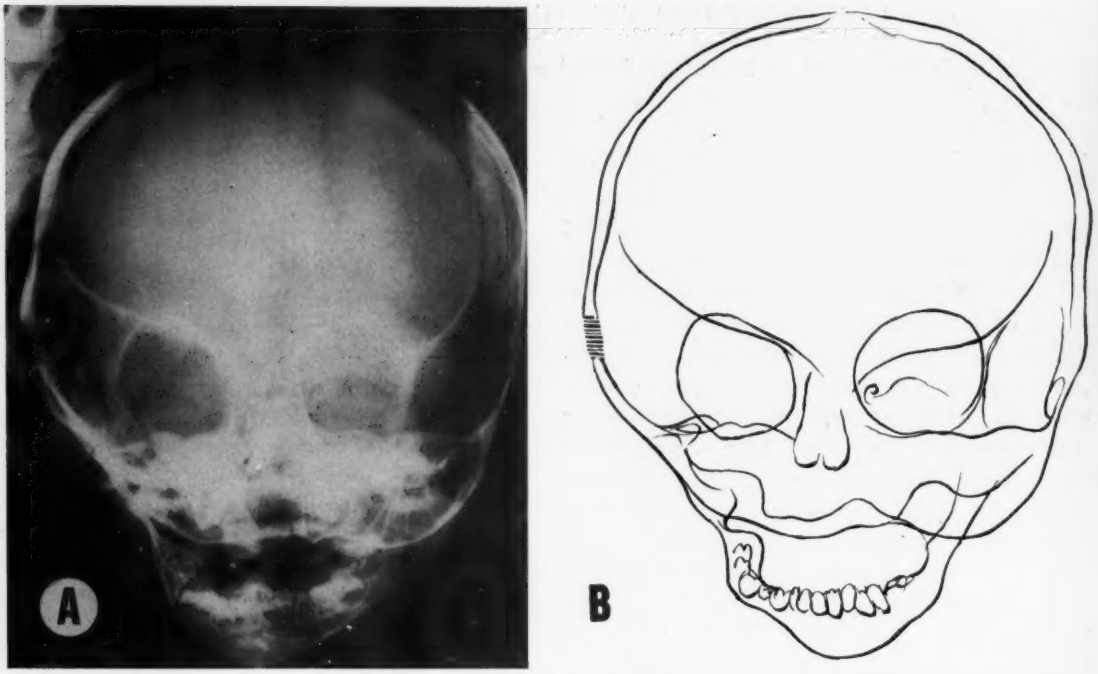

FIG. 1. Case 1. (*A*) Posteroanterior view of the skull showing absence of bony landmarks within the left orbit and bulge in the left temporal region with bony hiatus. (*B*) Line drawing of (*A*). Shaded area in left temporal bone indicates area of bony hiatus.

FIG. 2. Case 1. Towne projection demonstrating bulge and bony defect in the left temporal bone. Note the flared margin of the defect.

seen to a better advantage as could the flaring edges of the defect.

On February 28, 1949, an operation was performed by one of us (L.T.F.), a curved incision being made just anterior to the ear. The temporal muscle was very thin. This was incised and stripped from the area of the defect with the periosteum. The bony defect was about the size of the end of a thumb with the bony margins flaring outwardly. The underlying dura was thicker than normal and flared out around the edges of the bony defect. This was incised and a large collection of cerebrospinal fluid was found beneath the arachnoid underlying the defect, with an increase in the number and size of the blood vessels in this area. The dura was not only thicker but pinker on cut section so that its appearance suggested that it contained tumor. Two pieces were removed for microscopic examination. Some of the enlarged vessels on the surface of the cortex were coagulated. Further exploration showed that the lateral and superior wall of the bony orbit was absent.

The pathological report on the pieces of dura submitted for examination was as follows: "The specimen consists of a single piece of tissue

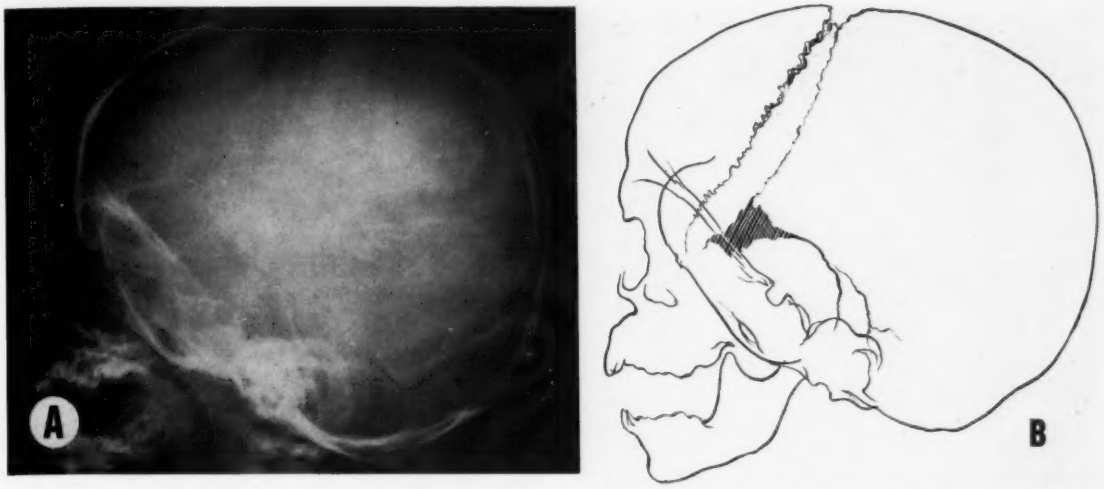

Fig. 3. Case 1. (*A*) Lateral view showing bony defect in left temporal region in the area usually occupied by the squamous portion of the greater wing of the sphenoid. (*B*) Line drawing of (*A*). Shaded region indicates area of bony defect.

about 1 cm. square and 4 mm. thick. One surface is composed of dense, gray, tough membrane and the other is ragged, dark red, softer tissue. Microscopically, there is dense collagen and is a little more cellular and slightly thicker than normal dura but there is no evidence of inflammation or neoplasm."

Comment. The roentgen appearance of the orbit was similar to the roentgenograms of the cases reported by Robertson[16] and those of LeWald[9] in that the usual bony structures in the orbit were absent. The mass in the left temporal fossa was undoubtedly due to the absence of that component of temporal wall contributed by the squamous portion of the greater wing of the sphenoid with consequent herniation of cerebral contents through it. LeWald[9] mentioned a case described by Schüller[19] in which the right temporal region was thinned and bulged outwardly and was associated with an absence of the upper and posterior portion of the bony orbit resulting in pulsating exophthalmos. Although Schüller thought this was a circumscribed destructive lesion due to a neoplasm, LeWald considered it another instance of defective development of the membranous bone in this region. A patient reported by Strandberg[20] and 2 patients reported by Rosendal [18] had a similar bulge in the temporal area due to a bony defect in the region of the sphenoparietal suture. Our patient had no clinical evidence of neurofibromatosis and the underlying vascular anomaly of the cortex was probably only coincidental.

Case II. J. H. (No. Y 610). This female infant was first seen at the age of four weeks because of a deformity in the region of the right eye which had been present since birth. Following a normal, full-term delivery the mother had noticed a bulging mass in the region of the bridge of the nose with slight proptosis of the right eye as well as lateral displacement. The left eye appeared normal. Examination at this time disclosed a bulging mass at the bridge of the nose with a large palpable bony defect at the inner edge of the left orbit which included the nasion, the medial portion of the roof of the left orbit, and all of the medial portion of the right orbital roof. The clinical impression was that of encephalocele. The head circumference measured 33 cm. At the age of eleven weeks the head circumference had increased to 38 cm. with the same measurement for the chest circumference. There was no apparent change in the mass at the bridge of the nose. The anterior fontanelle seemed large, measuring 4 by 5 cm.

She was next seen at the age of seven months when she seemed to be developing well, eating satisfactorily and gaining weight. The supra-

FIG. 4. Case II. Frontal view showing soft tissue mass at bulge of the nose.

orbital ridges were flat, and on both sides, where normally there would be a horizontal orbital roof, there was a depressed vertical wall instead. The soft tissue mass at the base of the nose seemed slightly larger than at the original examination.

On March 15, 1948, at the age of seven months, she was admitted to the hospital. Physical examination at this time revealed a prominent forehead, greater on the right than on the left and a small bulging mass in the area of the bridge of the nose which protruded, especially when the child cried (Fig. 4 and 5). The right eye was displaced laterally and forward and there was conjunctival chemosis medially. Ocular motility was normal and the examination of the fundi was negative. Palpation disclosed a bony defect involving the roofs of both orbits.

Roentgen examinations of the skull were carried out and disclosed a somewhat asymmetrical skull in the lateral projection with an increased vertical dimension (Fig. 7). The sutures, fontanelles, and sella turcica were all within normal limits. The frontal bone ended abruptly at the inferior portion of its squamous portion with apparent complete absence of the orbital portion (Fig. 6*A*). The nasal bones were formed normally but the nasal process of the frontal bone was completely absent. The frontal projection confirmed the findings seen in the lateral view, *i.e.*, absence of the orbital roof, superciliary arch and entire upper half of the orbit. The maxillae were not affected. The body and lesser wings of the sphenoid were present but the greater wings seemed to be wholly absent and no superior orbital fissure could be seen. In the Towne projection, one could again identify the lesser wings of the sphenoid. The irregular termination of the squamous portion of the frontal bone could be easily demonstrated about 6 cm. anterior to the anterior fontanelle.

On March 10, 1948, an operation was performed by one of us (L.T.F.) and a semicircular flap of periosteum exposing both supraorbital ridges was reflected. Laterally, there was a rudimentary supraorbital ridge on both sides, but medially the inferior aspect of what normally would be the supraorbital ridge was devoid of all bone so that the frontal bone was without any bony attachments to the orbital roof. The dura was stripped back exposing a complete absence of the orbital roof, bilaterally, as well as an absent cribriform plate, although the sphenoidal ridge was present on both sides. Anteriorly over the frontal lobes there was no true dura but a membrane which had intimately attached itself to the tissues in the orbit and to the tissues lining the floor of the anterior

FIG. 5. Case II. Lateral view.

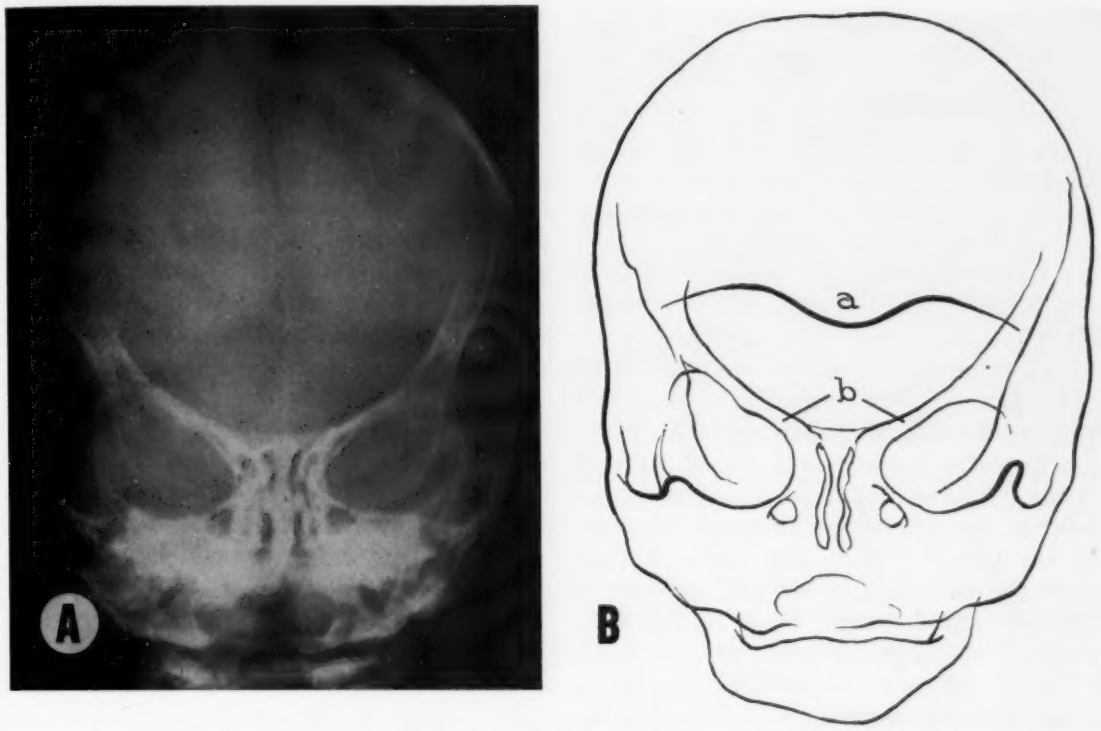

Fig. 6. Case II. (*A*) Posteroanterior view of the skull demonstrating absence of the upper half of both orbits and inferior portion of squamous portion of the frontal bone. Lesser wing of the sphenoid is present bilaterally. (*B*) Line drawing of (*A*). Line *a* represents the inferior border of the frontal bone; *b* indicates the lesser wings of the sphenoid.

fossa. This membrane was incised and the tip of the right frontal lobe elevated. This was found to extend into the defect and since it could not be readily freed, the tip was amputated. A diamond-shaped bone flap was reflected from the frontal bone and slipped under both frontal lobes, where it was allowed to rest on the lesser wings of the sphenoid and fastened with tantalum wires. Convalescence was uneventful and the subsequent development of the child was normal. When last seen, over two years after the operation, she was getting along well although her forehead was quite prominent due to the absence of a nasal bridge.

Comment. While this case did not present the diagnostic problem presented by Case I, it is of interest since it represents an extreme example of this condition in which practically the anterior one-half of the frontal bone was absent. This bony defect could be so readily palpated that the diagnosis could be made from the physical examination. Bilateral involvement was rare in the cases reported in the literature.

DISCUSSION

This anomaly consists essentially of an absence or failure of development of that portion of membranous bone which separates the cranial contents from those of

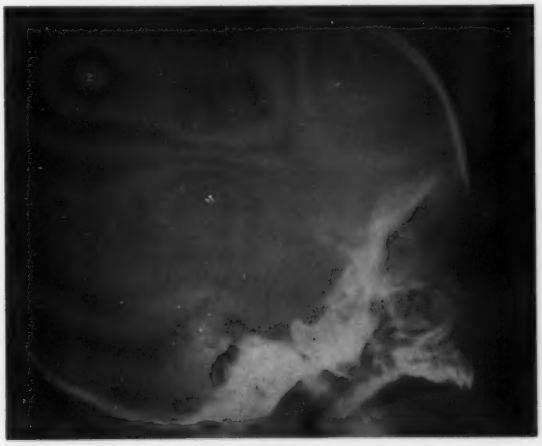

Fig. 7. Case II. Lateral view shows absence of the superior portion of the orbit and abrupt termination of lower portion of the frontal bone.

the orbit. If this defect is large enough, a portion of the cranial contents may prolapse into the orbit and displace the eye with resultant exophthalmos. When this occurs it may properly be called an orbital meningocele. Intraorbital meningoceles have been divided into anterior and posterior types.[23] The anterior type is the most common and emerges between the ethmoid and frontal bone at the expense of the horizontal plate of the ethmoid and passes between the frontal process of the frontal bone, lacrimal bone, cribriform plate and nasal process of the superior maxilla. It appears on the surface as a rounded sessile swelling in the upper inner angle of the orbit at the side of the bridge of the nose. In the posterior type the meninges may enter the orbit through natural openings or through an abnormal bony hiatus. The natural openings include the posterior ethmoid foramen, sphenoidal fissure or even the optic foramen as in the case reported by Cohen.[4] The abnormal bony defect may be due to bone destruction by disease or to incomplete bone formation as in the cases described above. Although there is usually a layer of dura separating the two chambers, intracranial pulsations may be transmitted to the contents of the orbit so that the exophthalmos is a pulsating one. Wheeler[21] cites Naffziger in saying that in patients who have had a portion of the orbital roof removed for malignant exophthalmos associated with hyperthyroidism, there may be pulsations of the eyes for a time although it tends to disappear. In cases of Schüller-Christian disease there may be similar orbital defects without pulsations but here the roof is replaced by dense fibrous tissue which resists pulsations.[21]

The first report of this condition was in 1904 by Rockliffe and Parsons,[17] although it was briefly mentioned by Clarke[3] in 1900. However, it was Dandy[5] in 1929 who first clearly described the condition in a fifteen year old girl who had had pulsating exophthalmos since birth. Roentgenograms demonstrated an absence of the posterior half of the orbital roof and this finding was confirmed at the time of surgery. A repair was done by inserting a piece of the outer table of the skull of the proper size and shape. LeWald[9] reported 4 cases in 1933, including the one previously reported by Dandy. In 1949, Strandberg[20] described a case of cephalocele of the posterior portion of the orbit whose characteristic roentgen features were similar to those described above. He was able to collect 31 cases from the literature, although the majority of the reports were by European authors. The most recent account was that of Robertson[16] who reviewed the literature and added 1 case of his own.

Relationship to Neurofibromatosis. In one of the earliest reports on this subject by Rockliffe and Parsons[17] in 1903 the patient was described as having a plexiform neuroma of the orbit with histopathological evidence of a neurofibroma in the orbit extending into the intracranial cavity. The authors did suggest the possibility that the bone defect in the orbital roof might have represented a failure of development. In most instances of this condition no orbital tumors have been present, although Anderson[1] mentions authors who described cases of pulsating exophthalmos where the condition was thought to be due to erosion of bone by a neurofibromatous mass. Moore[12] reported 4 cases of diffuse neurofibromatosis with proptosis but felt that the bony defect was more likely one of failure of development rather than bone destruction by a tumor. This association of an orbital defect with neurofibromatosis has been noted by many. Two of LeWald's cases had evidence of diffuse neurofibromatosis, although LeWald and Robertson felt that the presence of the neurofibromatosis was coincidental. A. E. Moore[11] described 2 cases in which neurofibromatosis was associated with proptosis and a defect of the orbital wall. Pfeiffer,[14] in describing 7 cases of neurofibromatosis of the orbit, stated that in 2 instances the bone separating the orbit from the intracranial cavity was lacking so that pulsating exophthalmos was present. In 1946 Peyton and Simmons[13] reported 5 cases of neurofibromatosis asso-

ciated with oribital wall defects and reviewed 20 other cases reported in the literature. Holt and Wright,[7] in studying a group of patients with neurofibromatosis, found a woman in whom plastic surgery had been performed for disfigurement of the eyelids but no osseous abnormality had been suspected. When skull films were taken not only were the walls of both orbits absent but the entire floor of the anterior cranial fossa was missing. A review of our own cases of neurofibromatosis resulted in a similar finding.

Case III. C. K. (No. 30829) (Courtesy of Dr. James B. Brown). The patient was a forty-five year old white woman with a history of multiple hospitalizations for plastic surgery on the right face and eyelid. Multiple subcutaneous nodules and a deformity of the right eyelid were first noted at the age of ten and the former had progressively increased in number and size. Biopsies of several of these nodules revealed them to be neurofibromata. At the time of her last hospital admission in 1949 examination disclosed pedunculated tumors over her entire body with numerous cafe au lait spots on the skin. On the right was a huge, soft, irregular, nontender tumor mass involving the eyelid and orbit. Roentgen examination of the orbits disclosed findings similar to those seen in Case I, *i.e.*, absence of the intraorbital bony landmarks (Fig. 8). Both the greater and lesser wing of the sphenoid were absent as well as the optic foramen, superior orbital fissure, and part of the orbital roof. Surgery was performed with removal of the tumor and the eye. At the time of operation it was noted that the bony roof of the right orbit was absent. Microscopic examination of the orbital tumor revealed neurofibrosarcoma. The patient later died of postoperative complications and at autopsy the right greater and lesser wing of the sphenoid and the right side of the sella turcica were found to be missing. Microscopic examination of sections taken from the region of the clinoid process showed no evidence of tumor invasion of bone.

Comment. The exact relationship of this condition to diffuse neurofibromatosis is not clear since it apparently has occurred in patients without any clinical manifestations of this disease. However, neurofibromatosis is now recognized as an inherited defect of many body tissues[10] and

Fig. 8. Case III. Detailed view of the orbits showing absence of bony landmarks in the right orbit. Note similarity to Figure 1.

three types of osseous alterations have been described as occurring in it:[7] bone defects or partial atrophy of bone; kyphoscoliosis and localized bone erosions resulting from pressure of a tumor and sometimes manifesting itself as a subperiosteal cyst.[2] Holt and Wright[7] state, "there is every reason to expect a high percentage of congenital anomalies in this disease (neurofibromatosis) which itself seems to result from some defect in the chromosomes and genes passed on to the individual by his forebears. In fact, some of the bone changes which have been described may be nothing more than associated anomalies." It seems highly probable that the absence of the orbital roof and greater and lesser wing of the sphenoid may represent one of these associated anomalies. Although in the 2 cases reported by us there was no clinical evidence of neurofibromatosis, it is conceivable that manifestations may occur later in life. Peyton and Simmons[13] emphasized that the cutaneous tumors and the pigmentation are only two manifestations of a congenital defect which may affect practically any or all of the systems of the body. Rosendal[18] reported 8 examples of cranial changes in neurofibromatosis: 2 cases in which the defects were localized to the optic foramen; 1 involving the sella; and 5 in which skull defects were present. Two of the latter had portions of the orbit missing

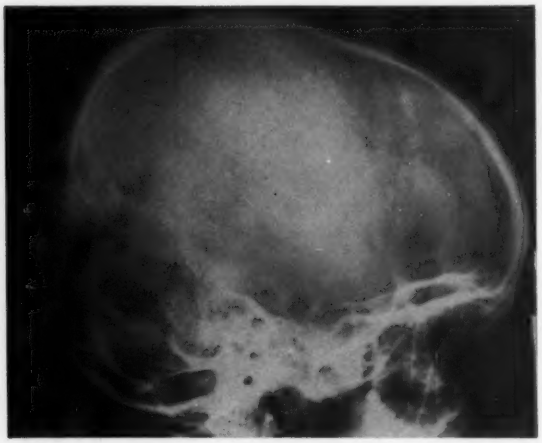

FIG. 9. Case IV. Lateral view of skull demonstrating oval defect in the right side of the occipital bone. Note smooth edges of the defect and normal adjacent bone.

as well as a thinning of the temporal bone with a bulge in the temporal fossa. Heine[6] described a case of neurofibromatosis with roentgen and subsequent autopsy proof of an absence of almost the entire half of the skull and facial bones. Defects occurring in the bony calvarium are illustrated by the following case.

CASE IV. (Courtesy of Dr. Alexis Hartman.) This nine year old boy was referred to Dr. Alexis Hartman because his mother had noted a soft spot in his skull. The boy had numerous cafe au lait spots and a few subcutaneous nodules. One of the latter proved to be a neurofibroma on biopsy. Both the father and paternal grandfather had definite evidence of neurofibromatosis and the child's mother had one cafe au lait spot on her forehead. Roentgenograms of the skull showed an oval defect on the right side of the occipital bone near the asterion which measured 2.5 by 3.5 cm., and two small irregular bone defects at the margin of the posterior fontanelle which measured 1.5 by 1.5 cm. and 1.5 by .5 cm., respectively (Fig. 9 and 10). The bone adjacent to these defects as well as the bone in the rest of the skull appeared perfectly normal. At surgery no abnormalities were found other than an area of absent bone corresponding to the roentgen findings.

Comment. It is our feeling that while the bone defects occurring in this disease are probably not due to bone destruction by neurofibromas, their occurrence in cases of neurofibromatosis has been too frequent to ignore a possible relationship and they may very likely represent a congenital defect which is one of the manifestations of this disease along with skin pigmentation and neurofibromas.

DIFFERENTIAL DIAGNOSIS

Since the roentgen findings are so characteristic, *i.e.*, absence of the usual bony landmarks in the orbit, the diagnosis should be made without much difficulty once one is aware of the existence of this entity, although any destructive process which involves bone might conceivably simulate it. Neoplasia, either primary or secondary, should be considered and, as mentioned before, this condition has been erroneously diagnosed as such. Xanthomatosis is well known to have a predilection for this portion of the skull but there are usually multiple areas of bone destruction elsewhere in the skull as well as in the rest of the skeleton. Dermoid tumors of the orbit should offer no difficulty in differentiation since they produce a discrete bony

FIG. 10. Case IV. Towne projection showing defect in right occipital bone and smaller defect near the region of the lambda.

defect with sharply defined sclerotic borders and tend to arise in the diploe but may produce a through and through defect.[15] Instances of eosinophilic granuloma involving the orbital roof have been described and this may be even associated with exophthalmos although of the nonpulsating variety.[22] Its appearance suggests a dermoid but it lacks the margins of increased density. Mucoceles are common in this area but can be demonstrated to communicate with the sinuses which are clouded. If pulsating exophthalmos is present one must consider the possibility of an arteriovenous aneurysm of the brain, orbit or cavernous sinus. In this condition there is usually a prominent bruit of which the patient is aware. A bruit is not usually present when pulsating exophthalmos is due to an orbital meningocele. R. F. Moore[12] operated on one such case for an arteriovenous fistula before he had recognized this feature.

SUMMARY

Two cases of defective bone formation in the region of the orbit have been discussed and the pertinent literature briefly reviewed. Examples of similar bone defects occurring in patients with neurofibromatosis have been presented. It is felt that such bone defects probably represent a manifestation of the multiple congenital anomalies found in neurofibromatosis. The roentgen characteristics of the defect have been described and the importance of its recognition is emphasized.

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NASOPHARYNGEAL FIBROSARCOMA IN A CHILD EXTENDING INTO THE CEREBELLOPONTINE ANGLE*

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NASOPHARYNGEAL tumors usually occur as epidermoid or undifferentiated carcinomas, lymphoepitheliomas or lymphosarcomas. Occasional cases of neuroblastoma, adenocarcinoma, chordoma, cylindroma and sarcoma presenting into this area have also been described.[1] These growths appear generally in the period from early adult life to old age. However, as indicated by Grotts[5] and Martin and Blady,[6] children may be similarly afflicted.

The present case concerns a three year old boy with a nasopharyngeal fibrosarcoma which extended into the posterior cranial cavity, producing a most interesting clinical, roentgenologic and pathologic picture.

REPORT OF A CASE

E.C. (Case No. 337841), a three year old boy, had been well until six weeks before admission. At first he complained of moderate abdominal pain which soon subsided. Two weeks later his parents noticed that his right eye was displaced so that "it went into the corner of the nose." Two weeks thereafter it was noted that his right eye was closed, that he did not walk properly and fell frequently. His speech changed and saliva drooled from the right side of his mouth.

When admitted, the child could not speak clearly and tended to repeat himself in conversation. He dragged his left leg when walking, and his left arm was kept in a semiflexed position. Facial weakness was present on the right side. The right eyelid was completely closed. The right pupil was larger than the left, both were regular, circular and reacted well to light. The right eye was fixed in midposition. Both optic discs were normal. The right corneal reflex was weak. Hearing on the right side was lost. The palate moved well but was deviated towards the right. The tongue protruded to the left but could be moved to either side.

There was considerable weakness of the left upper extremity, with a fine tremor of the hand and forearm. The finger-to-nose and the heel-to-leg tests were grossly abnormal bilaterally, with a marked deficit on the left side. The tendon reflexes in the upper and lower extremities were elicited bilaterally but were weaker on the right side. A positive Babinski response was obtained on the left side.

Physical examination was otherwise not remarkable. No lymph nodes were felt in the neck, and the nasopharynx appeared normal.

Lumbar tap revealed crystal clear fluid with a negative Pandy reaction. The protein content was not determined.

Plain skull roentgenograms showed no bone defects. The sella turcica was normal in size, configuration and bony density. The vascular and suture lines were normal. The petrous and sphenoidal ridges were intact. A soft tissue opacity in the nasopharynx was interpreted as adenoidal tissue, normal for the patient's age.

Ventriculography, including midline laminagrams, showed the lateral ventricles to be slightly enlarged, and shifted 4 mm. from right to left. The left occipital horn filled completely, while the right terminated sharply at a point 3 cm. from the atrium. The third ventricle did not appear to be dilated. Its anterior aspect was normal, but the posterior portion was displaced upwards as indicated by an aditus to posterior clinoid measurement of 4.5 cm. as compared with the normal adult range of from 3.0 to 4.0 cm.[4] The Sylvian aqueduct and the fourth ventricle filled completely with the patient in the brow-down position. On the midline laminagrams, however, only the middle third of the aqueduct was visualized in the same plane as the fourth ventricle, indicating that the course of this channel deviated from the midsagittal plane even though no obstruction was present.

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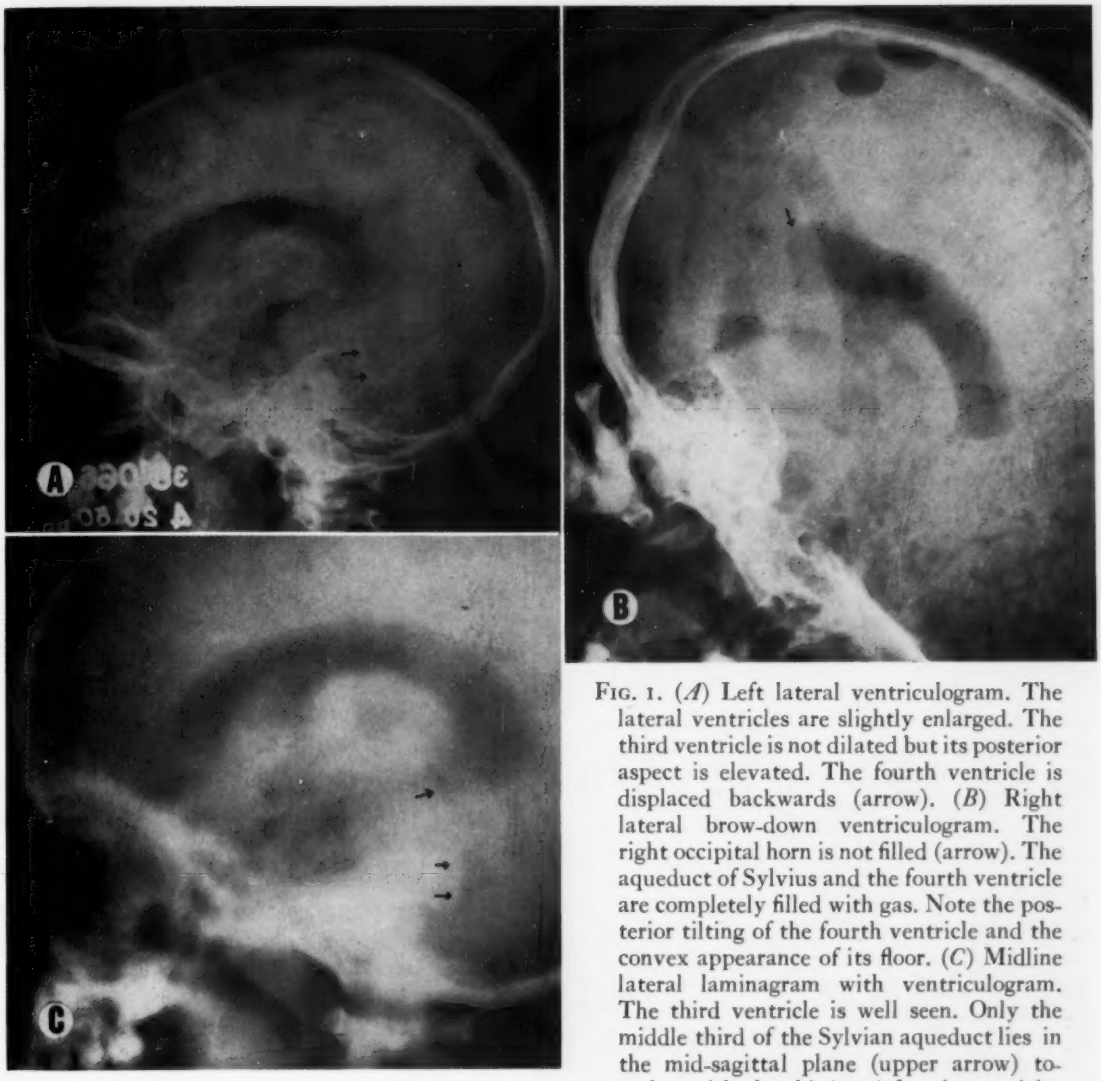

Fig. 1. (*A*) Left lateral ventriculogram. The lateral ventricles are slightly enlarged. The third ventricle is not dilated but its posterior aspect is elevated. The fourth ventricle is displaced backwards (arrow). (*B*) Right lateral brow-down ventriculogram. The right occipital horn is not filled (arrow). The aqueduct of Sylvius and the fourth ventricle are completely filled with gas. Note the posterior tilting of the fourth ventricle and the convex appearance of its floor. (*C*) Midline lateral laminagram with ventriculogram. The third ventricle is well seen. Only the middle third of the Sylvian aqueduct lies in the mid-sagittal plane (upper arrow) together with the third and fourth ventricles (lower arrows).

The fourth ventricle was displaced dorsally, the floor to dorsum measurement being 4.8 cm. as compared with a normal range of 3.0 to 4.0 cm. The chamber was narrowed, the fastigium to floor measurement being reduced to 1.0 cm. (normal range 1.5 to 2.0 cm.). The floor of the fourth ventricle presented an arcuate appearance convex posteriorly. The gas did not enter the basilar cisterns.

The clinical impression was right posterior fossa tumor. The ventriculograms were considered indicative of a pontine mass. The patient died before exploration of the posterior fossa could be accomplished.

Necropsy disclosed a completely unsuspected flat tumor of the posterior wall of the nasopharynx which had perforated the dorsum sellae, the clivus and the overlying dura. The basilar foramens were undisturbed. An intradural firm, globular, encapsulated mass 3.5 cm. in diameter was present in the posterior cranial fossa. This growth extended from the nasopharyngeal tumor and was attached to the dorsum sellae. It occupied the right cerebellopontine angle and extended across the midline, impinging against and flattening the pons and the adjacent brain stem without invading brain tissue. No other metastatic deposits were

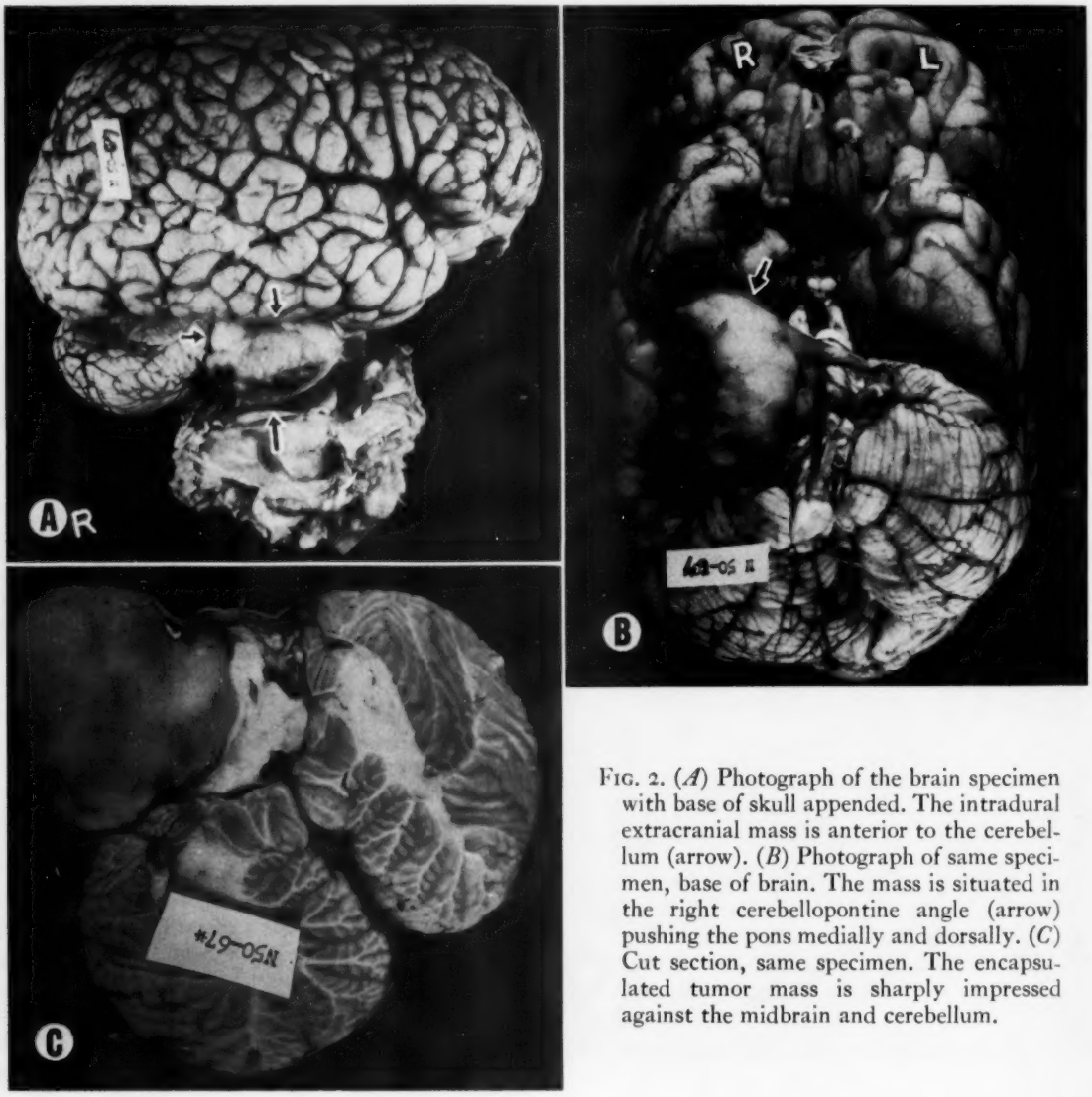

FIG. 2. (*A*) Photograph of the brain specimen with base of skull appended. The intradural extracranial mass is anterior to the cerebellum (arrow). (*B*) Photograph of same specimen, base of brain. The mass is situated in the right cerebellopontine angle (arrow) pushing the pons medially and dorsally. (*C*) Cut section, same specimen. The encapsulated tumor mass is sharply impressed against the midbrain and cerebellum.

found. On cut section the intracranial extension was gray-white, firm and friable. Sections taken from the base of the skull showed tumor cells on either side of the bone with neoplastic infiltration of the marrow. Histopathologically the growth was a periosteal fibrosarcoma.

COMMENT

Nasopharyngeal tumors are slow in producing discomfort, and usually manifest themselves by symptoms of nasal obstruction, bleeding, impaired hearing, localized pain and metastases to the cervical lymph nodes. Extension into the base of the skull may be followed by cranial nerve involvement. The present patient had no symptoms referable to the nose, nor were cervical lymph nodes present. The clinical picture was that of a posterior fossa tumor with no evidence of increased intracranial pressure, together with impairment of the third, fourth, fifth, sixth, seventh, eight and probably the twelfth cranial nerves. The plain skull films were normal but ventriculography disclosed changes in the Sylvian aqueduct, the fourth ventricle and the ipsilateral occipital horn which quite definitely pointed towards a posterior fossa

tumor, and which on second thought could be localized to the right cerebellopontine angle.[3] At necropsy an intradural mass contiguous with the nasopharyngeal fibrosarcoma was situated in this position.

Metastases from nasopharyngeal tumors frequently involve the base of the skull. Martin and Blady[6] believe that the usual route of such invasion is by direct continuity of the tumor through the foramen lacerum into the middle cranial fossa, the metastases tending to remain extradural and subperiosteal. They ascribe the destruction of bone to erosion resulting from extension of tumor enveloping the inner and outer tables of the base of the skull. Further progression of nasopharyngeal tumors through the carotid groove and supraorbital fissures may occur in a similar fashion. Cutler, Buschke and Cantril[2] stated that pharyngeal tumors may extend directly through the base of the skull without passing through existing foramens, and may lead to symptoms of increased intracranial pressure. The present case confirms this observation and further indicates that the growth may enter the posterior cranial fossa, remain encapsulated and exert its influence by compression rather than by invasion of brain tissue.

SUMMARY

A case of nasopharyngeal fibrosarcoma in a three year old boy is described. The tumor perforated the basiocciput, extended as a large, encapsulated, intradural mass to the right cerebellopontine angle and gave rise to a clinical picture of an atypical posterior fossa growth and a roentgenologic picture of an angle tumor without visible bone changes.

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MECKEL'S DIVERTICULUM*

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INTRODUCTION

MECKEL'S diverticulum is a congenital malformation resulting from the failure of normal obliteration of the fetal communication between the yolk sac and the midgut. At the end of the second week of embryonic life, there is a wide communication between the yolk sac or umbilical vesicle and the primitive intestinal tract. As growth continues, this communication gradually becomes narrowed and elongated, and there is an apparent progressive constriction of the embryo from the yolk sac. Under normal conditions this tube-like tract or vitelline duct obliterates, and the intestinal tract becomes completely separated from its previous connection with the yolk sac. This normal chain of regression may be halted or distorted and, depending upon the stage or manner in which this occurs, several types of anomalies may develop. The vitelline or omphalomesenteric duct may remain patent throughout, so that a fistulous communication exists between the ileum and the umbilicus. At the opposite extreme, only a fibrous band or vascular cord may be found, extending from the ileum to the undersurface of the umbilicus. In intermediate stages a portion only of the duct may persist or be patent. If the distal segment persists, a so-called umbilical cyst occurs, and this may or may not have fistulous communication with the umbilicus. Clinically, this must be differentiated from a patent urachus or urachal cyst. If the proximal portion of the duct persists and communicates with the ileum, a Meckel's diverticulum results. Of considerable interest, both embryologically and clinically, is the fact that while patent portions of the vitelline duct are lined with digestive tract mucosa, this mucosa is not necessarily of the ileal type. Gastric, duodenal and colonic type mucosa have also been described and the presence of pancreatic tissue has been reported.

Of the various anomalies resulting from the failure of normal obliteration of the vitelline duct, Meckel's diverticulum is by far the most common and is the only one which concerns us here. The anomaly is named after Johann Friedrich Meckel (1781–1833), a German physician who was Professor of Anatomy and Physiology at the University of Halle. He was not the first to describe the diverticulum or to suggest its origin, but he was the first to carefully study the anomaly and he wrote repeatedly upon the subject.[27,30]

It is the purpose of this article to analyze the autopsy, clinical and roentgenologic experience with Meckel's diverticulum in a large institution, and to present 2 cases in which the anomaly was demonstrated roentgenologically.

AUTOPSY, CLINICAL AND ROENTGENOLOGIC EXPERIENCE

1. *Autopsy Experience.* Most of the standard textbooks state that the diverticulum is present in 2 to 3 per cent of individuals coming to autopsy. Cunningham[3] reports that the lesion was present in 2.2 per cent of 3,302 bodies especially examined with reference to its existence. Haber[17] quotes numerous authors reporting on autopsy studies in which the incidence varies from 0.1 per cent to 2.7 per cent. Harkins[21] gathered from the literature several autopsy series totalling 24,149 examinations, in which the over-all incidence was 1.3 per cent. This is in accordance with our findings. In 10,000 consecutive autopsies at The Johns Hopkins

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Hospital (1929–1947) a total of 103 diverticula were recorded, an incidence of 1.0 per cent. In 27 of these 103 cases (25.9 per cent) there were other significant congenital malformations. Of the 103 diverticula, 77 were found in males and 26 in females, a ratio of 3:1 in favor of the males. This also is in keeping with Harkins series, in which 76 per cent were in males.

In none of our autopsy cases had the diverticulum been of any known clinical significance. Descriptions in the protocols are often relatively scanty, but in general the diverticula were innocent in appearance, almost all of them having wide ostia at their origin from the ileum and ending blindly. In only 1 case did the picture differ significantly. Here there was a fibrous band running from the tip of the diverticulum to the under surface of the umbilicus, where it joined a cystic structure containing golden mucoid fluid. In 1 diverticulum a fish bone was discovered. In all cases the diverticula apparently arose from the antemesenteric side of the ileum. This is the usual finding, although occasional cases have been reported in which the diverticulum seemed to arise from the mesenteric side and actually be enclosed within the mesentery.[43] In 68 of our autopsy cases the length of the diverticulum was stated. The longest measured 13.0 cm., the shortest 0.5 cm., and the average length was 3–4 cm. The distance of the diverticulum from the ileocecal valve was recorded in 75 instances. The greatest distance was 200 cm., the shortest 2 cm. and the average distance 80–85 cm. Infrequent reports are encountered in the literature of giant diverticula, but it is thought that most of these represent examples of intestinal reduplication rather than true Meckel's diverticula.[25,32] There is 1 seemingly well documented case in which a Meckel's diverticulum was found arising from the base of the appendix, with a vascular band connecting its tip to the underside of the umbilicus.[18] In only 20 of our 103 autopsy cases were adequate microscopic studies made. Of these, 13 were lined with small intestinal mucosa only. In 6 cases, gastric mucosa was identified, and in 1 case, the presence of pancreatic tissue was noted.

2. *Clinical Experience.* While Meckel's diverticulum is present in 1 to 2 per cent of the population, it would appear that the clinically significant incidence of the anomaly is relatively low. Over a twenty year period (1931–1950) only 19 Meckel's diverticula of proved clinical significance were encountered at The Johns Hopkins Hospital. During the same time period, 29 clinically insignificant diverticula were detected at laparotomy. The age of the patients with clinically significant diverticula, at the time they underwent exploratory laparotomy, is shown in Table 1.

Table I

AGE WHEN PATIENTS WITH CLINICALLY SIGNIFICANT MECKEL'S DIVERTICULA CAME TO SURGERY

Age in Years	No. Cases
0–2	7
3–10	4
11–20	4
21–30	1
31–40	3
41–	0
Total	19

It will be noted that in approximately one-third of the cases the anomaly made itself obvious during the first three years of life, and that slightly over half of the cases came to surgery during the first decade of life. This age distribution of symptomatic cases is in keeping with other reported series.[21,24,25] The sex distribution corresponds to the ratio found in autopsy experience, there being 15 males and 4 females.

The pathological complications of the significant cases are shown in Table II.

In 6 of the cases, it was severe bleeding which brought the patient to the hospital. In all of these, the blood was passed per rectum, the stools usually being dark red or tarry. The known duration of the bleeding varied from eight days to two years. In the more chronic cases, there was usually a

TABLE II

PATHOLOGICAL COMPLICATIONS OF MECKEL'S DIVERTICULA

Type of Pathology	No. Cases
Hemorrhage	6
Obstruction	6
Intussusception	4
Acute inflammation (with or without perforation)	3
Total	19

clear cut history of intermittent episodes of hemorrhage. All 6 patients had rather marked anemia. It is well recognized that there is a particularly high incidence of aberrant gastric mucosa in those diverticula which bleed, and this is also true in our series. In 4 of the 6 cases, the presence of gastric mucosa was detected microscopically, while in the remaining 2 cases the diverticulum was said to be lined with small intestinal mucosa only. In all but one case, an ulceration, presumably the source of the bleeding, was found. In 2 cases there was evidence of previous localized perforation, the perforation having been walled off by adjacent intestine or omentum. It has been commented upon in the literature that not infrequently a bleeding ulcer in a Meckel's diverticulum may go on to perforate.[29]

In 6 of the clinically significant cases, acute intestinal obstruction occurred. The duration of the symptoms varied from a few hours in most of the cases to five days in 1 individual. At operation, the obstruction in 3 individuals was found to be caused by a segment of small intestine being caught behind a loop formed by the attachment of the tip of the Meckel's diverticulum to some adjacent structure. It is of interest that gastric mucosa was found in all 3 of these cases, and it is probable that a previous ulceration or localized inflammatory reaction played a factor in the formation of the fibrous bands or adhesions. In 2 of the remaining cases of intestinal obstruction, the diverticulum was strangulated in a hernial sac; in both, the diverticulum was the only segment of intestine involved. In the remaining case of obstruction, the pedicle of the diverticulum had twisted upon itself, and the diverticulum was tense and gangrenous. Halstead, in 1902, gathered together from the literature 69 cases in which intestinal obstruction was associated with Meckel's diverticulum.[20] Almost invariably, the symptoms were acute, and by far the most common cause of the obstruction was the herniation of a loop of small intestine under a band formed by the diverticulum and its attachment to adjacent structures.

In 4 of our cases, the Meckel's diverticulum was the leading point of an intussusception. The duration of the symptoms ranged from one and a half to three days, and the clinical picture in each case was typical of intussusception. In 2 of these insussusceptions, a therapeutic reduction by means of a barium enema was attempted. In 1, it was obvious that the intussusception was incompletely reduced at the time of the examination, and the patient was immediately explored. In the other case, the intussusception either recurred or was not completely reduced, necessitating surgical intervention. In the remaining 2 intussusceptions, the patients were explored without roentgenologic studies. Harkins[21] collected 111 cases from the literature in which intussusception was due to an invaginated Meckel's diverticulum. He estimated that 17 per cent of Meckel's diverticula that cause symptoms do so by producing intussusception. Of interest is the fact that 27 of his cases occurred in individuals between the ages of twenty-one and fifty.

In the remaining 3 cases of clinically significant diverticula, inflammation, with or without perforation, brought the patients to the hospital. In all 3, the symptomatology was quite acute, and there was clinical evidence of peritoneal irritation. At exploratory laparotomy, in 1 case, there was a free perforation at the base of the diverticulum, and gastric mucosa was

present. In another case, the tip of the diverticulum was acutely inflamed, with omentum stuck to it, and gastric mucosa was found at its base. In the third case, there was a perforation, the opening being closed by omentum; only small intestinal mucosa was detected on microscopic study. Thompson[43] collected from the literature 36 cases of perforated ulcer in Meckel's diverticulum, and found that gastric mucosa had been present in 33, or 86 per cent. He points out that the ulceration usually occurs not in the aberrant gastric mucosa, but in neighboring small intestinal mucosa, either in the diverticulum or at its junction with the adjacent ileum.

While hemorrhage, obstruction, intussusception and acute inflammation account for most of the clinically significant Meckel's diverticula, a review of the literature reveals that other types of pathology have also been reported. Nygaard and Walters[35] in 1937 reviewed the literature on malignant neoplasms arising from Meckel's diverticula. They were able to find 20 cases, 14 being sarcomas and 6 carcinomas. They also comment on various benign neoplasms which may occur. Regional enteritis and tuberculosis have been described, although these processes have usually not been confined to the diverticulum.[22,31] Foreign body perforations of the diverticulum have been seen, the offending foreign body most often having been a fish bone and less frequently wooden splinters and needles.[28,45] Calculi have been found within Meckel's diverticula, and occasionally visualized on roentgenograms, but the calculi in themselves have seldom been of clinical significance.[13,34]

A correct preoperative diagnosis of pathology involving a Meckel's diverticulum is frequently not made. The preoperative diagnosis in our 19 clinically significant cases is presented in Table III.

It will be seen that in only 6 of the 19 cases was the correct diagnosis seriously considered. In 5 of these, the prominent clinical symptom was bleeding, and in the remaining case, obstruction was the presenting complaint.

Table III

PREOPERATIVE DIAGNOSIS IN CLINICALLY SIGNIFICANT CASES

Diagnosis	No. Cases
Meckel's diverticulum seriously considered	6
Acute appendicitis	5
Intussusception	4
Strangulated hernia	2
Perforated peptic ulcer	1
Bleeding peptic ulcer	1
Total	19

There was no mortality associated with any of our 19 cases, although several of the patients had rather stormy postoperative courses. In all, the diverticula were resected at the time of exploratory laparotomy.

3. *Roentgenologic Experience.* The roentgenologic experience with the 19 clinically significant cases is summarized in Table IV.

Table IV

ROENTGENOLOGIC STUDIES* IN CLINICALLY SIGNIFICANT CASES

Pathological Process	No. Cases in Which Studies Were Performed	Not performed
Hemorrhage	5	1
Obstruction	0	6
Intussusception	2	2
Inflammation	0	3
Total	7	12

* Consisting of small intestinal series and/or barium enemas.

It will be noted that in only 7 of the 19 cases were contrast roentgenologic studies of the intestinal tract attempted, either in the form of a small intestinal series or a barium enema. In 5 of the 7 cases in which such studies were performed hemorrhage was the predominant clinical feature. In the remaining 2 cases intussusceptions were present, and here emergency barium enemas were performed for therapeutic as

well as diagnostic purposes. In none of the 5 cases in which contrast studies were attempted, and in which the terminal ileum was visualized, was the Meckel's diverticulum indentified. Contrast roentgenologic studies were not performed in any of the 6 cases of obstruction or the 3 cases of acute inflammation. These cases were correctly considered to be surgical emergencies, and there were no indications for doing such examinations.

Pfahler[36] is generally given credit for having been the first to demonstrate a Meckel's diverticulum by roentgenographic means. He reported on 2 cases in 1934, only 1 of which was confirmed by laparotomy. His proven case was examined in 1923, and the diverticulum was visualized on a gastrointestinal series. Case,[8] in a general article on diverticula of the jejunum and ileum published in 1926, briefly mentions 1 case in which he made a correct preoperative diagnosis by roentgenologic means. Periodically since that time articles have appeared in the literature dealing with the roentgen demonstration of Meckel's diverticulum. Most of these have been brief case reports, and some have been so poorly documented as to be of no value. A reasonable search of the literature, however, reveals 20 additional instances in which a proved diverticulum was apparently demonstrated, and in which there is enough documentation to permit some analysis of the cases.* Of the total of 22 cases the diverticulum was demonstrated by a small intestinal series in 15 instances and by retrograde filling of the terminal ileum by barium enema in 5 instances; in 2 cases the anomaly was visualized on both a small intestinal series and a barium enema. In general, the small intestinal series consisted of periodic films, with or without accompanying roentgenoscopy, as the barium meal passed through the small intestine. The diverticulum was usually identified as a pouch-like collection of barium, there being considerable variation in the length of time that it remained filled. It was usually located in the lower abdomen or pelvis, and more often than not to the right of the midline. Peristaltic activity within the diverticulum was occasionally observed.

Fourteen of these demonstrated diverticula were of clinical significance, and the remaining 8 were either incidental findings or of dubious importance. In 11 of the 14 clinically significant cases hemorrhage was the predominant clinical finding. In 2 of the remaining cases, subacute obstruction was present, and in the final case a diverticulitis was found to be the cause of the patient's symptoms. The high incidence of hemorrhage in this group of roentgenologically demonstrated cases is of interest, since clinically the other pathological complications occur with equal frequency. It tends to bear out our experience that contrast roentgenologic studies were, for the most part, attempted only in those instances where hemorrhage was the predominant clinical finding.

The age span of the patients in the 22 cases of roentgenologically demonstrated diverticula ranged from seven and a half months to seventy-four years. Sixteen of the patients were above ten years of age. In the clinically significant group 6 of the patients were in the first decade of life, 3 were in the second and the remaining 5 cases were in the third decade or beyond.

Many of the standard roentgenologic textbooks, as well as many physicians writing on the clinical aspects of Meckel's diverticulum, state that the roentgen demonstration of the anomaly is so infrequent as to make the value of contrast roentgenologic studies almost worthless.[2,14,25,38] From the over-all standpoint it is difficult to argue against this contention. With standard roentgenologic techniques for studying the terminal ileum, the diverticulum is so uniformly overlooked that a negative roentgenologic report is of little significance. The presumed explanation is that the average Meckel's diverticulum,

* See references 1, 2, 4, 5, 7, 9, 10, 11, 15, 16, 19, 23, 26, 33, 37, 38, 39, 41, 42, 44, 46. Since this article was submitted for publication several other case reports have appeared in the literature.

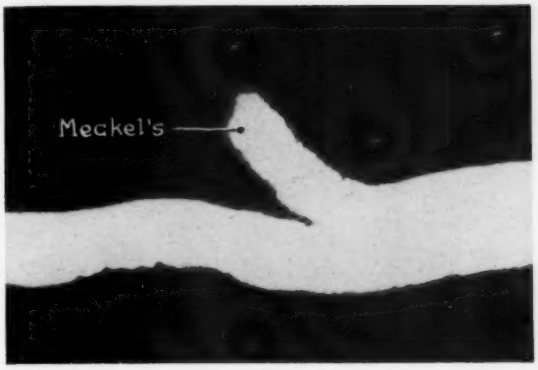


Fig. 1. Roentgenogram of a Meckel's diverticulum obtained during an autopsy on a three year old child. The relatively short length, wide ostium and lumen diameter comparable to the adjacent ileum are well shown.

with its relatively short length, wide ostium and a lumen diameter comparable to the adjacent small intestine cannot by ordinary methods be differentiated from adjacent small intestinal loops. This is well demonstrated in Figure 1, a roentgenogram of a Meckel's diverticulum obtained at autopsy from a three year old child.

The most spectacular claim for the roentgen demonstration of the diverticulum has been made by Good and Fletcher[15] of the Mayo Clinic. They state that in 11 out of 17 cases of Meckel's diverticulum an adequate study of the ileum was obtained. In 6 of these cases the presence of a pathological condition was detected, and in 4 instances the diverticulum was identified. These statements are made in a general article on the roentgenologic examination of the small intestine, and only 1 case is discussed in any detail.

It should be pointed out that noncontrast roentgenologic studies, including horizontal and erect views of the abdomen, may be of value in demonstrating the presence of acute intestinal obstruction or perforation secondary to a Meckel's diverticulum.[6]

REPORT OF CASES

Case 1. The patient, J.U. (J.H.H. No. 561732) was a white male, aged seventeen, admitted for the first time to The Johns Hopkins Hospital on January 21, 1951, for evaluation of gastrointestinal bleeding. The family history was noncontributory. The past history revealed that the patient had always been weak and sickly. At the age of two there was an episode of possible intestinal obstruction during which a mass was noted in the right side of the abdomen. The possibility of intussusception or parasitic infection was said to have been considered at that time by a pediatrician. After an enema the symptoms subsided, and there is some question as to whether or not parasites were found in the stools. Following this there were recurring episodes of vomiting and abdominal pain until the age of nine, at which time an appendectomy was performed. A "large appendix" was found, and thereafter the abdominal episodes were infrequent.

The onset of the present illness was not well defined. Approximately four months prior to his current hospital admission, the patient went to his local physician because of a severe cold. At that time it was noted that he was quite pale, and the presence of anemia was confirmed by blood studies. Stools were positive for blood, and on questioning, the patient stated that his stools were frequently black and tarry. Because of the anemia and evidence of bleeding he was hospitalized elsewhere for further study. Roentgenologic studies of the gastrointestinal tract were said to have been unrevealing, and the patient's family was informed that the site and cause of the bleeding were unknown. For a few weeks preceding the present hospital admission, the patient had noticed a progressive increase in weakness, exertional dyspnea, dizziness and headache. There were a few dull, vague abdominal aches which were not well localized.

On physical examination, the patient was moderately well developed and nourished. There was marked pallor of the skin and mucous membrances. The heart was not enlarged, but a soft systolic murmur was heard over the entire precordium. No masses or abnormalities were detected within the abdomen, and rectal examination revealed no pathological process.

Initial laboratory studies revealed a marked hypochromic microcytic anemia, with a red blood cell count of 2.73 million and a hemoglobin of 5.7 gm. Guaiac test of the stool was strongly positive for blood, but no ova or parasites were found.

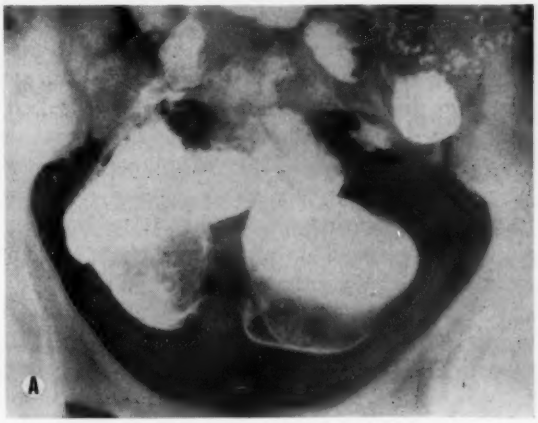
FIG. 2. Case 1. Reproductions of the one and two hour roentgenograms, showing the diverticulum lying well down in the pelvis.

The original impression was that the patient probably had some specific bleeding lesion within the gastrointestinal tract, but that the nature of the lesion could not be determined from the information then available.

A barium enema was thought to reveal no gross lesion in the colon or terminal ileum, although the cecum was not well visualized because of residual feces, and it was suggested that the examination be repeated. A gastrointestinal series three days later revealed no pathological condition of the esophagus, stomach or duodenal bulb. There was some slight distortion of the descending portion of the duodenal loop, but this was thought probably to be of no clinical significance. Hourly films and roentgenoscopy revealed a bizarre appearing dilated segment of small intestine lying well down in the pelvis (Fig. 2 and 3). Its depth within the pelvis was such that it could not be manipulated by palpation, and it exhibited no peristaltic activity during roentgenoscopic study. While it could be identified on the one through five hour films it did not seem to be a point of any significant obstruction, since the proximal small intestine was not dilated and the barium meal started to enter the cecum at the end of three hours. The terminal ileum appeared grossly normal, and there was too much fecal material in the cecum for accurate evaluation of this structure. A twenty-four hour film revealed no residual barium within the peculiar small intestinal segment. The roentgenographic impression was as follows: "There is a definite abnormality of a segment of the small intestine, probably ileum. In view of the patients's history, it would be interesting to speculate upon the possibility of Meckel's diverticulum or a reduplication. Another possibility would be adhesions, perhaps from the previous surgery, causing some minimal degree of obstruction to a loop of ileum. The apparent kink in the descending portion of the duodenal loop may well be of no clinical significance."

It was felt that in view of the clinical and roentgenologic findings an exploratory laparotomy was indicated, and this was performed on February 2, 1951. A large Meckel's diverticulum was found, arising from the antemesenteric border of the ileum approximately 40 cm. from the ileocecal valve. It measured 9 cm. in length by 5 cm. in greatest width, and there

was a circular constriction in its mid-portion. The neck of the sac was so widely patent that it did not seem feasible to perform a simple diverticulectomy, and therefore the ileum was divided transversely on either side of the diverticulum so that both the diverticulum and the ileum from which it arose were removed (Fig. 4). An end-to-end anastomosis was then performed between the remaining ileal loops. On opening the specimen and diverticulum was seen to be lined throughout with mucosa (Fig. 5). There were several superficial petechial mucosal hemorrhages, but no gross ulcerations or hemorrhagic areas were found. The mucosal folds were fairly well developed, and their distribution is well demonstrated in Figure 4. Microscopic sections from the ileum and the two pouch-like segments of the diverticulum revealed normal small intestinal mucosa, and



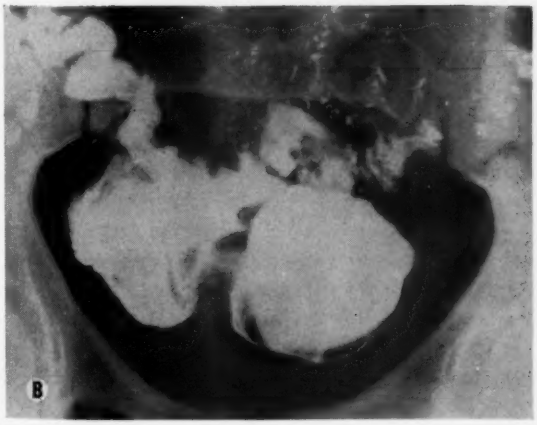
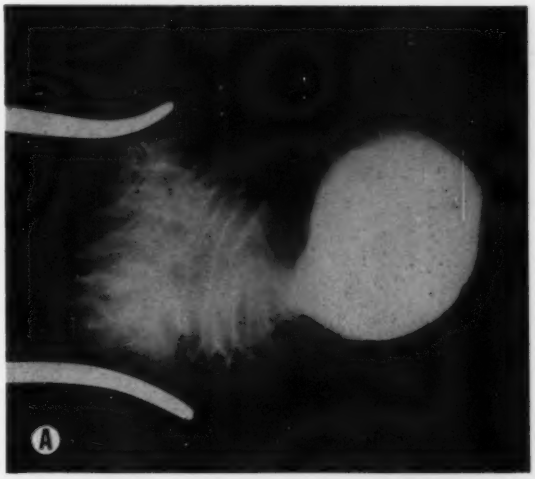


Fig. 3. Case 1. Close-up views of the diverticulum taken from the three and four hour films. The constriction in the mid-portion of the diverticulum is well shown (compare with Fig. 4).



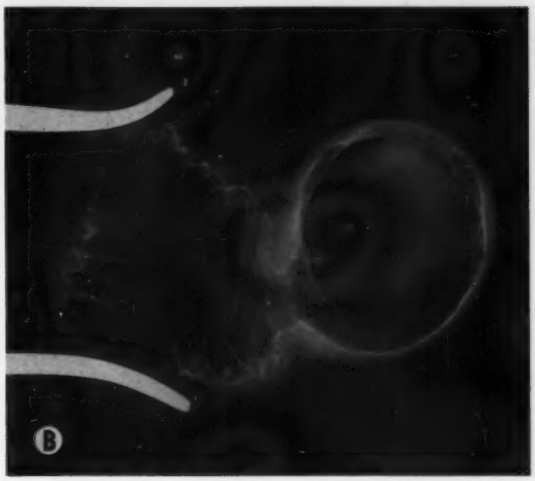


Fig. 4. Case 1. Roentgenograms of the operative specimen. Clamps have been placed across the free ends of the ileum on each side of the diverticulum. Note the wide ostium of the diverticulum at its origin from the ileum, and the constriction in its mid-portion.

no gastric or aberrant tissue was detected. There was a virtual absence of submucosa in the distal pouch of the diverticulum, and here the muscular layer was indistinctly divided into circular and longitudinal bundles. No inflammatory changes were noted.

The patient's postoperative course was reasonably smooth. During his stay he received supportive therapy for his anemia in the form of transfusions and intravenous administration of feojectin. Shortly after discharge the patient returned to his home in another state. In a follow-up letter ten months after surgery his mother stated that he had gained 25 pounds,

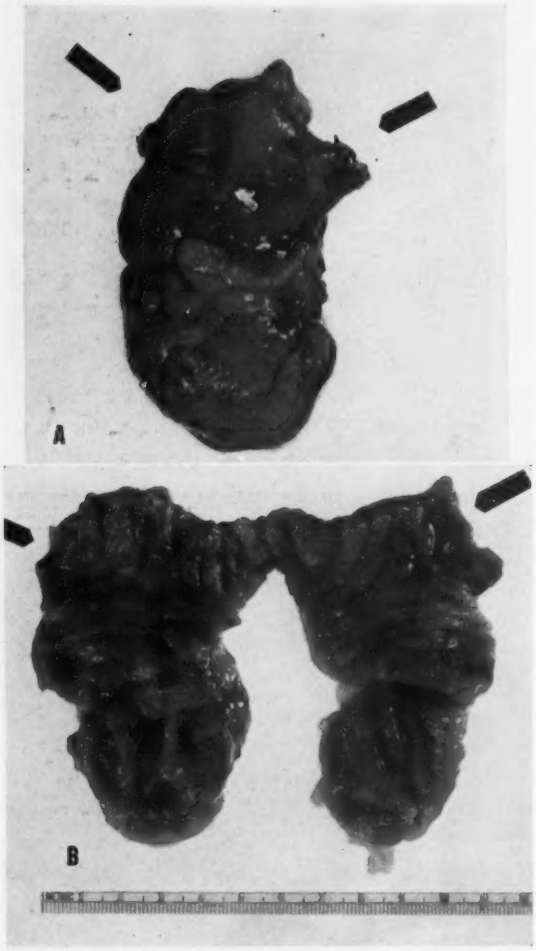


FIG. 5. Case I. Photographs of the intact and opened operative specimen. The arrows indicate the free ends of the ileum on each side of the diverticulum. The constriction of the lumen in the mid-portion of the diverticulum was not obvious from the external surface.

was stronger than he had been in all his life, and that there had been no further evidence of bleeding.

CASE II. The patient, W.P. (J.H.H. No. 600333) was a white female, aged forty-four, admitted for the first time to The Johns Hopkins Hospital on March 11, 1952, for evaluation of abdominal pain and a right upper quadrant mass. The family and past histories were noncontributory. The present illness dated from 1948, at which time she first developed attacks of pain in the right upper quadrant. A gastrointestinal series done elsewhere is said to have revealed the presence of a deformed duodenal bulb. She was slso found to have *Amoeba histolytica* in her stools, and was treated for these with carbasone. On an ulcer diet the abdominal pain disappeared, and she was essentially well until late in 1951, when the pain recurred. It was then quite severe, occasionally radiating to the right subscapular area, and was not related to meals or relieved by alkali or and ulcer diet. There was some vomiting, the vomitus on several occasions having a coffee colored appearance. She had lost 15 pounds in weight. The positive physical findings on admission were limited to the abdomen, where a poorly defined mass was palpated in the right upper quadrant. Laboratory studies revealed a hematocrit of 40.5, and a hemoglobin of 12.0 grams. Stool and gastric aspiration specimens were guaiac positive.

A barium enema on March 14, 1952, revealed no intrinsic pathology in the colon, nor was there any displacement of the hepatic flexure by the mass detected clinically. The terminal ileum was filled and no abnormalities were observed roentgenoscopically. On the posteroanterior filled film of the colon, however, there was an apparent diverticulum coming off the terminal ileum overlying the body of the fifth lumbar vertebra (Fig. 6). This tubular structure measured roughly 3 by 0.5 cm., and save for its unusual location, one would have thought that it represented the appendix. There was no evidence, however, that it communicated with the cecum, and the vermiform appendix was not filled. In the remaining films the apparent diverticulum was obscured by overlying barium-filled intestinal loops. In the roentgen report it was stated that the possibility of a Meckel's diverticulum should be considered, and it was requested that this anomaly be looked for if the patient underwent an exploratory laparotomy. A gastrointestinal series three days later revealed a partially obstructed stomach, with an irritable and deformed duodenal bulb. Because of the obstruction an attempted small intestinal study was unsuccessful.

On March 24, 1952, an exploratory laparotomy was performed by Dr. William Grose. An inflammatory mass, the size of a tennis ball, was found involving the duodenum and head of the pancreas. This was secondary to a large penetrating duodenal ulcer, and it was elected to perform a subdiaphragmatic vagotomy and anterior gastroenterostomy. The terminal ileum was also examined, and a Meckel's diverticulum was found approximately 18 inches from the ileocecal valve. It was somewhat atypical in that it arose from the ileum immediately adjacent to the mesenteric border, rather than

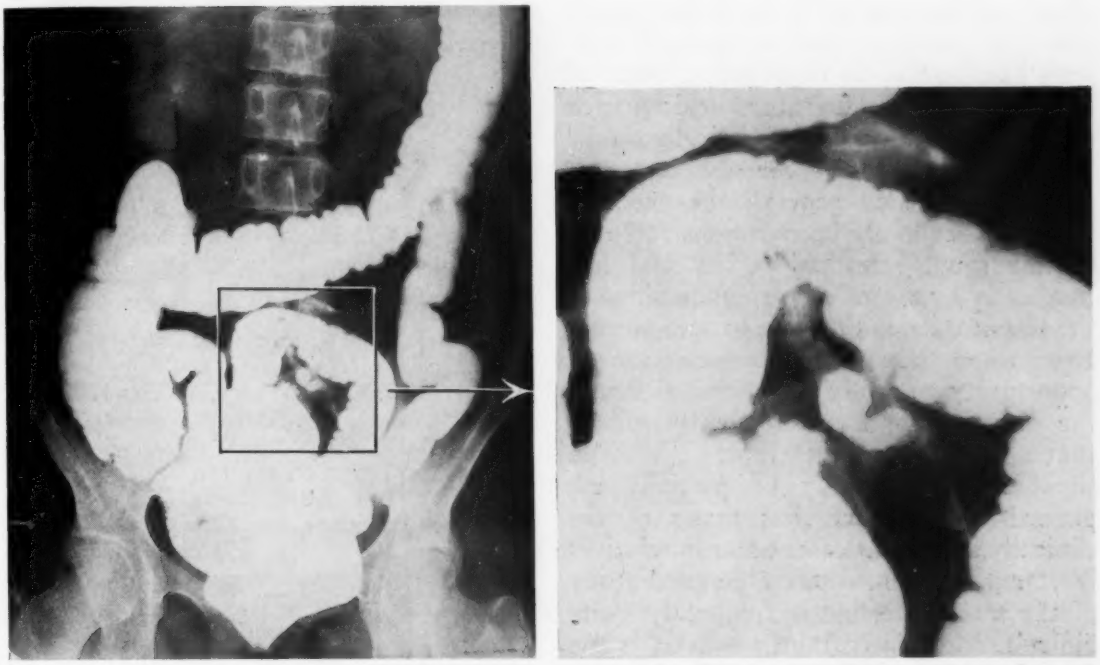


Fig. 6. Case 11. Reproductions from the posteroanterior filled film of the colon, showing the diverticulum overlying the body of the fifth lumbar vertebra.

from the antimesenteric side. It had the appearance of a small appendix, with its own mesentery and accompanying blood supply arising from the parent ileal mesentery. Its tip was completely free in the abdominal cavity. A simple diverticulectomy was performed. A small innocent-appearing vermiform appendix with an obliterated lumen was also resected. Pathological study of the diverticulum revealed that it was 3.5 cm. in length, with a patent lumen varying from 1.0 cm. in diameter at its base to 0.5 cm. at its tip. It was lined by normal appearing small intestinal mucosa, no aberrant tissue being detected. The muscular layer was rather thin.

The patient's postoperative course was uneventful, and she was discharged from the hospital on the fourteenth postoperative day.

DISCUSSION AND SUMMARY

Meckel's diverticulum, the most common anomaly resulting from the failure of normal obliteration of the vitelline duct, is present in 1 to 2 per cent of the population at large. In 10,000 consecutive autopsies its presence was recorded in 103 instances, or 1 per cent, and there was a three to one ratio in favor of males.

It is relatively uncommon for the diverticulum to assume any clincial significance. In The Johns Hopkins Hospital only 19 such cases were found over a period of twenty years. The chief pathological complications which occur with the anomaly are hemorrhage, obstruction, intussusception and acute inflammation, and these are most prone to occur in the first decade of life. The presence of aberrant gastric mucosa within the diverticulum appears to favor the development of many of these complications.

The roentgenologic demonstration of Meckel's diverticulum continues to be a relatively uncommon occurrence. In the clinically significant cases, the radiologist seldom has an opportunity to carefully study the terminal ileum. Those cases with acute obstruction, intussusception and inflammation are truly emergencies, and here a therapeutic barium enema for the reduction of an intussusception is usually the only justification for attempting contrast roentgenologic studies. Those cases in which bleeding is the predominant clinical symptom frequently pursue a less

acute course, and it is here that small intestinal series or barium enemas may with justification be undertaken. Most of the reports in the literature dealing with roentgen demonstration of clinically significant diverticula have occurred in instances of hemorrhage. In general, the anomaly has most frequently been demonstrated on routine small intestinal series, and less frequently by means of retrograde filling of the terminal ileum during a barium enema. Even when the radiologist does have an opportunity to study the terminal ileum, the diverticulum is so frequently missed that a negative roentgen report is of little significance. This may be partially explained by the fact that many of the clinically significant cases occur in relatively young children, where a detailed study of the small intestine is frequently quite difficult. More important, however, is the fact that the average Meckel's diverticulum does not lend itself to easy recognition by roentgenologic means, regardless of its clinical significance. Its short length, wide ostium and a lumen diameter comparable to the adjacent ileum tend to make its identification difficult. It is the atypical diverticulum, such as was found in the cases reported here, that one has the best opportunity to identify.

In spite of the rather poor showing that roentgenology has made as a means of identifying Meckel's diverticulum, it is felt that, in cases of unexplained bleeding from the lower gastrointestinal tract in adolescents or adults, a careful study of the terminal ileum is justified, since it is in this group of cases that the diagnosis has usually been made. Theoretically, one would expect that some of the special techniques for examining the small intestine, including careful and frequent roentgenoscopy, might offer the best opportunity for identifying the diverticulum.

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THE ANATOMY OF THE PYLORIC CANAL AND THE ETIOLOGY OF INFANTILE PYLORIC STENOSIS

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IT HAS long been known that the roentgen appearance in infantile pyloric stenosis represents a stage in the movements of the normal stomach (Forssell, 1932). It is, according to this author, reason to assume that the condition is due to an abnormal function of the autoplastic closing mechanism of the pyloric canal in which the mucous membrane, through the torus pyloricus functionalis, participates to the same extent as the contraction and the stratification of the muscularis propria. Forssell conceives of this torus pyloricus functionalis as a functional parallel to the mucous membrane torus which is prominent in some species, for example in the pig.

A representation of some results of more recent studies of the anatomy of this section of the stomach by Torgersen (1942), and Wernstedt (1943, 1944) may be justified. The conformity of the observations is evidence of their validity. The observations are further confirmed by the comparative anatomical investigations of the first author. As these observations may be of interest to the radiologist dealing with pyloric stenosis in daily work, I will discuss them briefly in the following. They may be of particular interest in connection with a discussion of a rare malformation of the stomach, representing in a way the counterpoint of infantile pyloric stenosis.

The roentgen appearance has been dealt with in a masterly way by Runström (1939). He distinguishes between three stages. In the first stage no peristalsis is seen and the emptying effect is small. In the second stage there is still no peristalsis, a few mucosal folds may be seen in the canal and the emptying function has improved. In the third stage are seen slight peristaltic movements.

In the dog (Fig. 1) the pyloric canal is limited by two sphincters, an aboral one analogous to the so-called pyloric sphincter in man, and an oral one. The two muscular loops or sphincters radiate from the pyloric sulcus on the lesser curvature side and embrace the greater curvature at a distance from each other of 3 to 5 centimeters. On the lesser curvature they unite to a low muscle knot in which the fibers intermingle. The circular fibers between the loops are fixed partly in the oral, partly in the aboral sphincteric loop. The interrelation between the sphincters depends on the asymmetrical position of the pyloric sulcus which lies closer to the angulus on the lesser curvature. The longitudinal musculature originates from the intermuscular connective tissue of the oral loop. They form caudally convex loops radiating upwards into the connective tissue of the pyloric sphincter. The longitudinal musculature is most powerful on the greater curvature side where the sphincters are most strongly developed. Identical anatomical relations are found in the rabbit. The longitudinal mus-

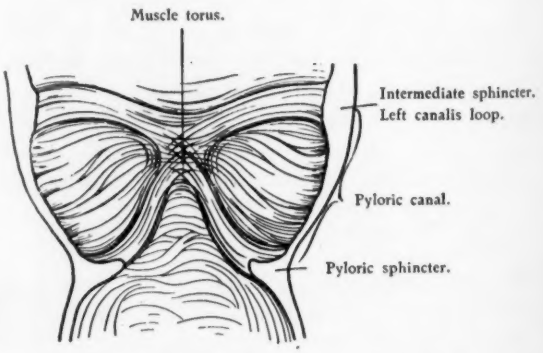

FIG. 1.* Pyloric canal in the dog. Note the muscle knot on the lesser curvature side. (Torgersen, 1942.)

* Figures 1, 2, 3, 4 and 5 are reproduced from the monograph of the author. Johan Torgersen: The Muscular Build and Movements of the Stomach and the Duodenal Bulb. *Acta radiol.*, 1942, Supp. 45, pp. 191.

culature is limited strictly to the region between the two sphincters in this animal. The similarity of the roentgen picture in a case of pyloric spasm in a dog and in infantile pyloric stenosis is good evidence that the double sphincter in the dog corresponds to the pyloric canal in man (Fig. 2).

In the pig (Fig. 3), the most obvious finding is the mucous membrane torus on the lesser curvature side. The two muscular sphincters are seen, delimiting an area in which the circular musculature has the same structure as in the dog. It may be reasonable to call the muscle knot where the sphincters intermingle on the lesser

Fig. 2. Pyloric spasm in the dog. (Torgersen, 1942.)

curvature side, the muscle torus. It corresponds to the mucous membrane torus. Numerous fibers radiate from the muscle torus into the mucous membrane torus, indicating that they form a functional unit. The muscle torus in the pig, contrary to that in the dog, hardly rises over the musculature of the duodenum. Numerous circular fibers from the duodenum run into the mucous membrane torus. Longitudinal musculature is developed on the greater curvature side and on the anterior and posterior wall, not on the lesser curvature, corresponding to the thickness of the pyloric sphincter (Fig. 4).

In man, as in the animals examined, the pyloric sulcus lies closer to the angulus on

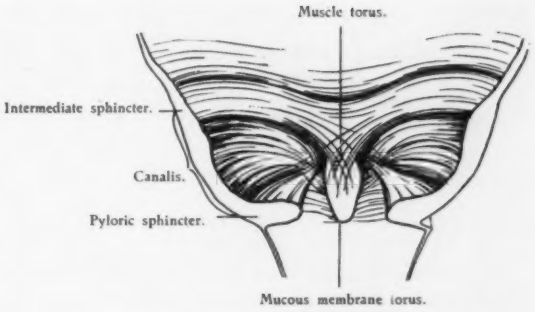

Fig. 3. The pyloric canal in the pig. (Torgersen, 1942.)

the lesser curvature side (Fig. 5). The pyloric canal is built in the same manner as in the animals recorded. The pyloric sphincter is continuous on the lesser curvature with a considerably wider oral loop, which is not so well defined as in the dog. However, the structure of the pyloric canal is rather variable also in the dog, the double sphincter not being so marked as in the above figure in all cases. The muscle torus is more powerful in man than in the dog, and much more powerful than in the pig. The longitudinal fibers have the same relation to the two sphincters in man as in the animals recorded. They become abruptly more numerous at the oral loop, forming a powerful band between the two loops on the greater curvature side. The conception of the double sphincter in man is not based on the study of the human stomach alone. A comparison with other species reveals the analogy and the existence of a double pyloric sphincter also in man.

Fig. 4. The longitudinal musculature in the canalis of the pig. (Torgersen, 1942.)

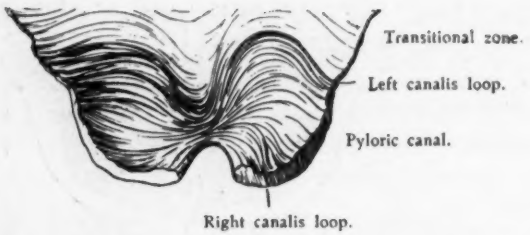

Fig. 5. The pyloric canal in man. Note the convergence of the circular fibers toward the lesser curvature side. (Torgersen, 1942.)

The circular fibers at the base of the duodenum join the sphincter pylori, separated from it on the greater curvature by a connective tissue septum. The sphincter pylori is composed of a larger gastric part and a considerably smaller duodenal part.

The relation between the muscle torus and the mucous membrane torus is in accord with regular rules. When the muscle torus is flat as in the pig, the mucous membrane torus is large. When the former is large, no mucous membrane torus is present, except functionally, as in man. There are in animals transitions between these extremes. As in the cat the mucous membrane torus may be substituted by mucosal folds.

The pyloric canal often forms the muscular stomachs in lower vertebrates. The significance of the oral sphincter is demonstrated by the fact that the greatest swelling of the musculature frequently lies orally to the pyloric valve of the mucosa. In the proper pyloric valve there is frequently no thickening of the musculature at all.

The fact that the roentgen picture in infantile pyloric stenosis may persist for years after the manifest stage is evidence that a malformation of the pyloric canal is one component in the etiology. This is confirmed by the statement of Runström (1939), that the roentgen picture also may be demonstrated before the onset of the symptoms.

There is good evidence that the disease is relatively frequent in first born and in boys and that these children are taller than the average and belong, for the most part, to the slender type when examined as grown-ups (Salmi, 1941). The observations of familial occurrence are convincing evidence of a hereditary factor, but the attempts so far to interpret the data by a single factor mechanism have not been successful.

In the comparative anatomical study I came to the conclusion that the varying build of the musculature of the stomach in vertebrates apparently was due to the relative growth of the layers of the stomach. The mucous membrane was supposed to grow faster than the musculature, expanding the latter and attenuating the mesodermal sheet of the stomach. The thickness of the musculature and course of the fibers therefore depend on the rate and direction of the growth of the mucous membrane. This supposition does not exclude other factors in the development of the muscular structure, nor does it presume anything about the nature of these influences whether they are mechanical or chemical or if they are related to the tonic function of the musculature. In case of the pyloric canal, the asymmetry of the pyloric sphincter and the thickness of the musculature may be assumed to depend on a different growth rate of the curvatures and on the relative fixation and low growth rate towards the transition to the midgut. In short, the anatomy of the stomach, according to this theory, should depend on the position of the organ in development, on its embryonic topography.

In a study of situs inversus in Norway, I came across a pair of dizygotic twins, one of whom showed complete situs inversus, the other an isolated inversion of the stomach. It is hardly possible to decide whether the liver is on the left or on the right side. The position of the organ is abnormally symmetrical. The shape of the stomach is peculiar. The lesser curvature is shorter than usual and the transverse stomach placed horizontally, the angulus

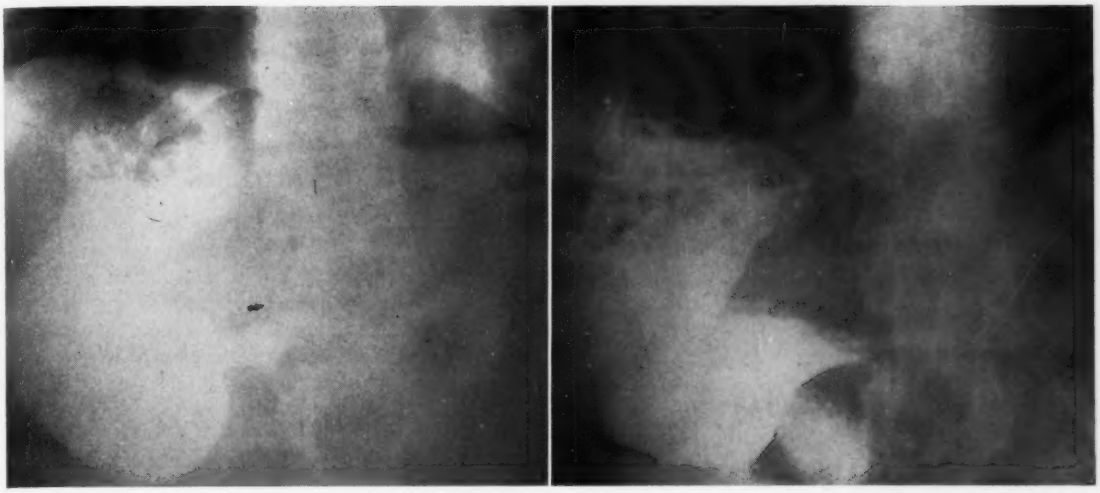

Fig. 6. Isolated inversion of the stomach. The heart is on the left. Note the relatively short lesser curvature and the high position of the angulus.

being positioned higher than usual (Fig. 6).

In his studies of partial inversion (1926, 1928), Pernkopf mentions 3 of these extremely rare cases of inversion of the stomach. What surprised him was that he found no trace of a pyloric sphincter in 2 of the cases. The transition from the stomach to the duodenum showed no differentiation of the musculature or the mucosal pattern. The pyloric canal looked like the small intestine. In one of the cases he found a very thick pyloric musculature. This case showed the unique combination of a stomach in the inverse situs, a duodenum in the normal situs. For this reason there was a very sharp angle at the transition from the stomach to the duodenum.

As far as I know, similar observations have not been recorded in the normal situs. Two of the cases represent a counterpoint to the infantile pyloric stenosis. Taken together they confirm the supposition that the embryonic topography is a decisive factor in the development of the pyloric canal and in infantile pyloric stenosis.

The factors in visceral asymmetry are fundamental in the determination of the position of the stomach during development. This is evident even from the few observations above. In the studies of the genetics of visceral inversion and the associated anomalies, I came to the conclusion that the situs of the viscera depends on a complex of genes that may be broken up in components particularly influencing the different organs (Torgersen, 1947).

These genes may be conceived of as modifiers influencing the asymmetry and consequently the structure of the organs. This interpretation does not exclude the influence of single genes. On the other hand, the body build of these children and the sex distribution indicate the influence also of modifiers with a rather general effect on growth and sexual differentiation. In case of pyloric stenosis, these modifiers may be assumed to have favored a development towards an abnormal degree of asymmetry. The counterpoint of the anomaly is observed in abnormal symmetry. In Pernkopf's cases is seen a pyloric canal with a muscular structure favorable to peristalsis, in infantile pyloric stenosis a canal favorable to the sphincteric function.

This conception of the etiology of pyloric stenosis does not exclude the influence of other factors in the disease. The intention of the present paper is to point out the importance of one particular factor in the etiology.

SUMMARY

The pyloric canal in man and several animals examined shows an analogous structure. This section of the stomach may be conceived of as being constituted by two sphincters. The aboral sphincter, which corresponds to the sphincter pylori, consists of a gastric and a duodenal part. The relationship between the musculature and the mucous membrane accords with general rules, indicating the functional relationship between them.

The varying structure of the musculature of the stomachs in the animals examined is indicative that the relative growth of the layers and the direction of growth are decisive factors in the development of the muscular pattern. The embryological topography of the organ may be supposed to be fundamental in the development of the muscular structure.

Concerning the observation of a case of isolated inversion of the stomach, in which the transverse stomach showed a rather peculiar shape, Pernkopf's observations on isolated inversion of the stomach are noted. In some of these cases the pyloric canal was found to be abnormal, twice showing an appearance which may be regarded as a counterpoint of infantile pyloric stenosis. The bearing of these observations on the etiology of pyloric stenosis is discussed with particular regard to the modifying effect of the factors in the development of the asymmetry of the viscera.

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Vol. 71, No. 1

VOLVULUS OF THE SPLENIC FLEXURE OF THE COLON*

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WE ARE reporting 2 cases of volvulus of the splenic flexure of the colon which we believe to be the first on record. The American and European literature does not record any reports of volvulus of the splenic flexure of the colon. Reports of volvulus of the sigmoid colon and cecum are frequent in the American literature and numerous in the European literature which also records a few cases of volvulus of the transverse colon.[1]

The statistics on the incidence and location of all types of colonic volvulus in the United States and Europe have been previously analyzed by Gerwig.[3] Olivier and Libaude[7] were able to collect only 16 cases of volvulus of the transverse colon from the literature up to 1948. They reported an additional case.

Volvulus of the colon, not in the sigmoid portion, is often associated with a congenital anomaly or an acquired defect. Volvulus of the cecum occurs with an abnormality of rotation or mesenteric attachment. Volvulus of the transverse colon has been present with total volvulus of the midgut[2] and in volvulus of the entire proximal half of the colon, associated with a cecal volvulus.[8] Murray[6] reported volvulus of the distal half of the ascending colon and the proximal two-thirds of the transverse colon occurring as a complication of labor. Martin and Ward[5] described volvulus of the transverse colon associated with megacolon and an adhesion across the transverse mesocolon. Groth[4] demonstrated an axial torsion of the colon occurring with a "physiological volvulus" of the transverse colon.

The rarity of this abnormality is easily understood when one considers the shortness of the mesocolon in the region of the transverse colon and the widely separated points of attachment of the hepatic and splenic flexures. This is exactly the reverse of what is frequently found in volvulus of the sigmoid colon.

Our patients with volvulus of the splenic flexure showed a clinical course similar to volvulus elsewhere in the colon. The chronic, intermittent complaints of moderate severity in these cases suggest that a partial volvulus of the splenic flexure could be the obscure cause of chronic bloating, constipation, and gurgling so frequently encountered in patients with no demonstrable abnormality. It is readily seen from Case II that such a condition could be reduced easily by a barium enema and thus go unrecognized.

The roentgenographic findings in these patients were identical with those of volvulus of the sigmoid colon. These have been completely described by Ritvo and Golden.[9]

REPORT OF CASES

CASE I. M.S., a female, aged seventy-eight, complained of six weeks of aching pain in the left upper quadrant, becoming progressively worse. Five days before admission she ate too much and she had three or four large stools the next day, followed by obstipation. On admission, the left upper quadrant pain had become stabbing in character. A barium enema had been administered before admission following which the patient had expelled a considerable amount of gas.

Past history revealed that she had had irregular bowel habits since she was ten. Ten years before admission she had diarrhea and constipation which had increased in severity. In 1906 she had had an appendectomy and in 1916 a hysterectomy.

On admission, the patient was not in acute distress. The abdomen was distended and

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FIG. 1. Case I. Barium enema showing volvulus of the splenic flexure with tapering of the lumen at the site of the twisting and the typical spiral bands of mucosa indicating torsion of the colon.

FIG. 2. Case I. Oblique view emphasizing findings of Figure 1.

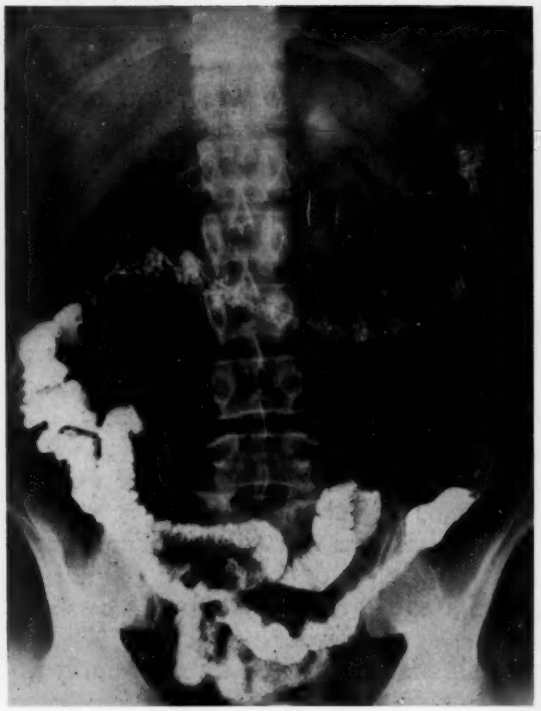

FIG. 3. Case II. Roentgenogram after discharge of the barium enema showing a normal splenic flexure.

tympanitic. Tenderness was localized to the left upper quadrant.

A barium enema demonstrated a volvulus of the splenic flexure without complete obstruction (Fig. 1 and 2).

At operation numerous adhesions were seen, one of which, a thick band, extended from the lateral wall of the abdomen to the transverse colon and enveloped the splenic flexure. The splenic flexure was incarcerated and rotated within this encasement. After freeing the band, the volvulus was reduced and normal mobility of the colon was restored. Constipation has been her only complaint since.

CASE II. V. W., a female, aged fifty-three, entered the hospital because of rectal bleeding for a period of three years. She was frequently constipated, and at those times she noted a low back pain with a drawing sensation radiating down her legs. These symptoms were relieved by defecation. In 1927 she had an appendec-

Fig. 4. Case II. Roentgenogram taken twenty-four hours after Figure 3 showing 180° torsion of the splenic flexure, which is dilated with gas.

tomy and a cholecystectomy, and in 1946 a hysterectomy.

At proctoscopic examination hemorrhoids were seen to be the source of the bleeding. A routine barium enema revealed no abnormality (Fig. 3). A roentgenogram taken twenty-four hours later revealed a volvulus of the splenic flexure (Fig. 4). This patient has not been operated upon for the volvulus.

SUMMARY

The rarity of volvulus of the colon other than in the sigmoid and cecal regions is discussed. Two cases of a hitherto unreported condition of volvulus of the splenic flexure of the colon are described and roentgenographic demonstrations of the abnormality are given.

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CALCIFICATION OF THE PORTAL AND SPLENIC VEINS*

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THE etiology of abdominal venous thrombosis is not clear and its incidence is low. When confined to this area, venous calcification, with the exception of phlebolith formation, is rare. Morgagni (1769) noted the first case of calcification of the inferior vena cava and Baillie (1793) described a similar finding. Lobstein is given credit for the initial description of intra-abdominal phlebosclerosis and calcification in 1833.

Despite its antiquity, no clearcut explanation exists. We have recently encountered a case of extensive calcification of the portal and splenic veins and have noted that only 21 cases[1,4,7,8,9,10,11] have been mentioned previously in the literature of the past fifty years. For that reason we are reporting our case. It is of interest to note that the first similarly reported case to be diagnosed roentgenographically and proven by surgery, occurred as recently as 1948.[1]

CASE REPORT

A white male, aged forty-two, letter carrier, was perfectly well until early in January, 1951, at which time he noticed anorexia, a persistent cough and a general malaise. Shortly after this, he had two episodes of hematemesis and melena. Within a few days after the hematemesis, peripheral edema and ascites developed. The patient stated that he might have been jaundiced at that time. He was admitted to another hospital, where a diagnosis of cirrhosis of the liver with esophageal varices, splenomegaly and secondary anemia was made. He was transfused and put on a low salt diet. The malaise improved and the ascites diminished. However, because of the findings of calcific shadows in the abdomen and persistent, marked splenomegaly, the patient was transferred to the Brooklyn Veterans Administration Hospital on March 23, 1951, for further study.

The past history showed that, since his return from the service in 1945, the patient had had a moderate to marked alcoholic intake, and a qualitatively and quantitatively poor diet. There was no history of jaundice, clay colored stools, dark urine or anorexia, but the patient was told six years before admission, while in the Army, that he had prominence of abdominal veins, "such as is often seen in liver disease." There was no history of exposure to rats or chemicals. The remainder of the past history was essentially negative.

Physical Examination. Physical examination, on admission, showed a well developed, somewhat undernourished white male, weighing 137 pounds; pulse 86, blood pressure 120/80, temperature 98.5° F. The pertinent physical findings included the presence of several small spider angiomas and prominence of a superficial vein running from the umbilicus to the xiphoid process. The spleen was enlarged, with the lower border 15 cm. below the costal margin. The liver edge was thin and nontender, and was located 7 cm. below the right costal margin. There was no evidence of ascites.

Laboratory and Roentgen Findings. On admission the white blood cell count was 5,800, with 62 per cent polymorphonuclears, 22 per cent lymphocytes, 2 per cent bands, 4 per cent monocytes and 10 per cent eosinophils. The red blood cell count was 3.7 million, hemoglobin 9.6 grams. Urinalysis was negative. Blood urea nitrogen was 17.9 mg. per cent. Prothrombin time was 20.2 seconds with a control of 12.5 sec.; cephalin flocculation 4+; thymol turbidity 8.3 units; bromsulphalein 19 per cent retention (45 min.); van den Bergh test, total 2.87 mg. per cent, with a direct of 0.35 mg. per cent; cholesterol 278 mg. per cent, cholesterol

* Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

esters 214 mg. per cent. Echinococcus skin test was negative and stools were consistently negative for bile and blood.

Roentgen examination of the abdomen revealed the presence of a large irregular transverse calcific mass in the mid-epigastrium, and a cystic mass in the left upper quadrant, in the area of the left lobe of the liver. There were also several smaller calcific masses in the right mid-abdomen (Fig. 1). The presence of esophageal varices and a large spleen were also noted.

Course in Hospital. The patient was asymptomatic on admission and the slight icterus which was present at that time cleared rapidly. He was able to walk and his liver function improved. He was ready for discharge three months after admission, when increasing icterus again appeared. Five days later the patient had a chill, followed by a temperature elevation to 103° F. This represented the only significant elevation throughout the entire hospital course. On this day, the total serum bilirubin climbed to 28.3 mg. per cent, with a direct of 5.33 mg. per cent, from a previous total of 0.99 mg. per cent, with a direct of 0.15 mg. per cent; thymol turbidity was 2.9 units and the alkaline phosphatase 51.6 King-Armstrong units. Following this, there was increasingly severe and unremittent icterus, disappearance of the previously noted hepatic mass, no change in the size of the left upper quadrant mass, and appearance of some ascites. The urine continued to be dark brown, but the color of the feces alternated between dark brown and clay colored. He lost approximately 9 pounds in weight, despite the appearance of ascitic fluid, and developed progressive anorexia and weakness. He continued on a rapidly retrogressive course with a rise of the total serum bilirubin to 45.5 mg. per cent, with a direct reaction of 14.5 mg. per cent; an alkaline phosphatase of 24.1 King-Armstrong units and a cholesterol of 87 mg. per cent, with 48 mg. per cent cholesterol esters. One week later the patient died in a cholemic state.

Autopsy Findings. The significant findings at autopsy were limited to the abdomen. There was a moderate amount of icteric fluid in the abdominal cavity. The liver was grossly deformed, weighed 1,700 grams and measured 30 by 12 by 10 cm. It was yellow-brown in color and bile stained. Three distinct types of surface markings were present: (a) a generalized small granular appearance; (b) a larger nodular cobble stone appearance; (c) several large gray-white depressed zones. On cut section, the cobble stone areas varied from 3 mm. to 1 cm. in diameter and were surrounded by depressed gray bands of tissue. Within the liver parenchyma and corresponding to the depressed scarred areas were irregular stellate gray bands of tissue 3 to 6 cm. in length. These were situated in the anterior portion and surface of the right lobe and the posterior region of the left lobe.

Fig. 1. Flat film of the abdomen showing extensive calcification of the portal and splenic veins.

Microscopic Findings. Liver: The normal architecture of the liver was greatly altered in some areas which corresponded mostly to the depressed zones in the right lobe of the liver. Occupying and replacing much of the liver parenchyma in these areas were loose and dense zones of connective tissue in which only remnants of bile ducts were present. Within this connective tissue were many dilated capillaries and diffuse collections of lymphocytes, polymorphonuclear leukocytes, fibroblasts and histiocytes and, toward the periphery, small round foci of liver parenchyma. Throughout the areas of fibrosis, the arteries and veins showed irregular intimal thickening of their walls by connective tissue. Some of the bile capillaries in these areas

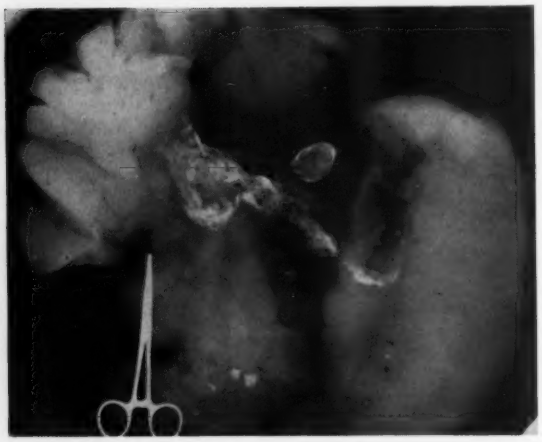

FIG. 2. Roentgenogram of the gross autopsy specimen of the liver, spleen and portal vein. This illustrates the extensive calcification and correlates the antemortem roentgen findings (Fig. 1.)

were distended with brown granular pigment. Similar but less extensive areas were noted throughout the remainder of the liver (Fig. 4). In other areas the liver had maintained its normal lobular architecture. Here the liver cord cells were irregular in size and shape and contained brown granular pigment.

Reticulum stain showed preservation of compressed reticular fibers in the areas of advanced fibrosis. Diagnosis: Postnecrotic cirrhosis.

The wall of the portal vein within the liver was of average thickness and in areas contained an occasional stony hard yellow zone varying in diameter from 3 to 5 mm.

The extrahepatic portal and lienal veins were greatly altered by the presence of stony hard yellow zones which lined the surface and protruded into the lumens. The walls of these vessels varied in thickness from 1 to 1.5 mm. and were firm and gray in appearance. The circumferences of the vessels were enlarged to 6.5 cm. in areas (Fig. 2).

Similar thickening, dilatation and calcium deposition were present to a lesser extent in the tributaries of the splenic vein.

A similar process also involved the superior mesenteric vein to a lesser but more diffuse extent (Fig. 2).

Microscopic Findings. The normal architecture of the portal vein and its tributaries was greatly altered by an increase of dense hyalinized connective tissue and bands of collagen fibrils in its intimal portion. Present here were many irregular calcium deposits. The endothelial lining of these vessels was frequently interrupted, and where so absent, moderately well organized thrombi were attached to the intima.

In many areas the entire wall was replaced by connective tissue and calcific deposits. The van Gieson stain showed absence or decrease of elastic fibers (Fig. 3).

Similar change was noted in the areas of aneurysmal dilatation of the splenic vein tributaries. Diagnosis: Phlebosclerosis with calcification, dilatation and thrombosis.

The spleen weighed 1,700 grams and measured 30 by 15 by 6 cm. It was reddish-purple in color and the capsule was thickened. On cut section the stroma was firm with minimal pulp scrapings and an increase in fibrous trabeculae.

Other significant findings were: (a) chronic passive congestion and fibrosis of the spleen; (b) esophageal and gastric varicosities; (c) bile nephrosis; (d) normal appendix.

DISCUSSION

This case presents several unusual features, the most outstanding of which is the extensive venous calcification. As stated previously, only 21 cases have been reported in the literature. These cases all refer to calcification of the vessel wall and must be distinguished from calcification of a thrombus within an otherwise normal or thickened portal vein. The latter is a much more common finding.

According to experimental work,[3] two underlying factors are necessary to cause venous calcification: (a) increased venous

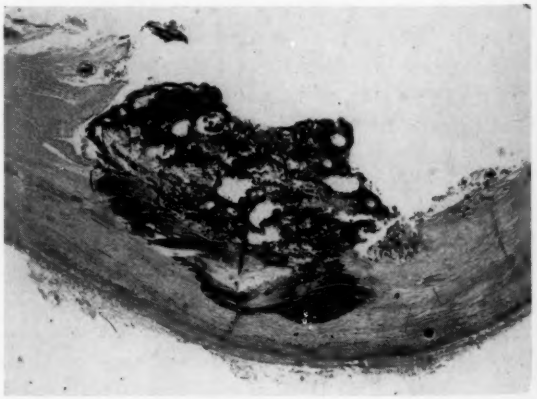

FIG. 3. Photomicrograph (10×) of the portal vein illustrating the extensive calcification of the wall with destruction of the elastic fibers and replacement by connective tissue (van Gieson stain).

pressure, and (b) disease of the vessel wall, causing nutritional disturbance and weakening. Clinically and experimentally, increased pressure alone does not cause calcification, and it is only very late in its course that phlebosclerosis occurs. The classical findings in this condition, then, are thickening of the intima and hypertrophy of the media.[3] In the late stages, fibrosis of the intima occurs, but calcification is not seen.

The literature bears this out, particularly as it applies to the portal system. The majority of cases reported were found prior to 1915 and a definite infectious process has most often been described. Syphilis and pyelophlebitis are the most common causes. Other factors contributing to this condition are alteration in the composition of the blood, alteration in blood flow and contiguous infections.[8] Perhaps the better control of infectious diseases, particularly syphilis, accounts for the decreased incidence in recent years.

The exact explanation in our case cannot definitely be attributed to any one of the above processes, but may be sought in a combination of some of them. From the postmortem findings there is little doubt that an old hepatitis existed. Whether this was on a bacterial or viral basis cannot be ascertained. However, it does appear that this infection was primary in the liver, since there are no history or autopsy findings suggesting a pelvic abscess, appendicitis with ascending pyelophlebitis or other source of a secondary ascending infection. As to the possibility of a primary bacterial hepatitis, this is also somewhat untenable as the latter usually causes a stormy clinical course such as was not elicited in the history of this case. On the other hand, virus hepatitis may run a chronic low grade course, resulting in clinically undetected, extensive postnecrotic cirrhosis.

It has also been shown,[5] that virus hepatitis frequently causes an endophlebitis in the hepatic vessels. We believe that such an event occurred in this patient and resulted in a retrograde infection of the portal and splenic veins. Thus, these vessels, damaged and weakened by the inflammatory process and subjected to a marked increase in pressure as a result of the intrahepatic venous obstruction, went on to extensive dilatation and calcification.

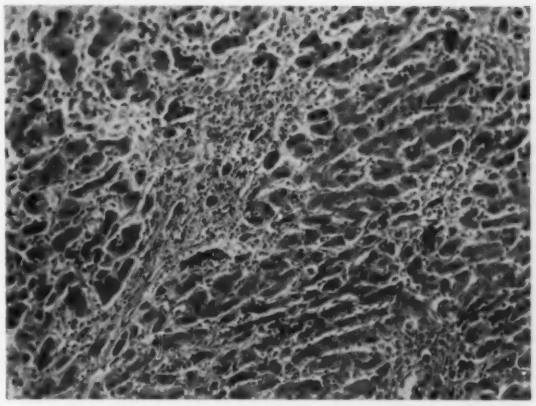

Fig. 4. Photomicrograph (150×) of the liver showing an irregular increase in connective tissue containing lymphocytic collections and an apparent reduplication of the bile ducts. Note the alteration in the liver cord cells.

The events as related to the patient's last hospital admission represent the terminal phase of an overdistended collateral circulation and complete liver failure. This was caused by an active hepatitis superimposed on the already extensively damaged liver. The reason for this may be found either in a reactivation of the old infection or a new process, which might have been introduced by blood transfusions received prior to admission.

On the basis of the above consideration, it is our impression that this is a case of portal and splenic vein sclerosis with calcification, representing an unusual late complication of infectious hepatitis.[2]

SUMMARY

1. A case of calcification of the portal and splenic veins is presented with the gross and microscopic findings.

2. The pathogenesis of this finding is discussed, and it is our feeling that this is an unusual sequence to hepatitis.

3. The confirmation of the roentgen findings adds another factor to the arma-

mentarium in the diagnosis of intra-abdominal calcification.

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We wish to thank Dr. Oscar Auerbach for his helpful suggestions and criticism.

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CASE OF BULLET IN HEART WITH RECOVERY

A THIRTY YEAR FOLLOW-UP

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY reported in June, 1923, "Case of Bullet in Heart with Recovery."[1] A follow-up of the same case more than thirty years later is now possible.

Excerpts from the original article relates that on February 17, 1919, a fifty-nine year old man attempted suicide by shooting himself with a .32 caliber revolver, the revolver being placed against the left chest.

Examination within a few minutes after the accident revealed a bullet wound in the fifth intercostal space, one-half inch to the left of the sternum. The patient was unconscious, deeply cyanosed, no pulse was perceptible and no heart tones could be heard.

The patient was given 1/60 gr. of strychnine sulphate hypodermatically and removed to the hospital. He soon regained consciousness, the pulse returned, and in three to four hours he was asymptomatic, except for severe pain in the chest. On March 4, 1919, fifteen days after admittance, he was discharged from the hospital.

On March 11, 1919, the patient was roentgenoscoped and the bullet was visualized just posterior to the wound of entrance and within the shadow of the heart, approximately midway between the right and left borders and approximately 2 cm. below the greatest diameter. There was an oblique movement of the foreign body with each cardiac impulse. In the lateral view, the foreign body was noted to be 1 cm. anterior to the mid-axis of the heart shadow. Subsequent anteroposterior and lateral films revealed the foreign body well within the shadow of the heart.

A second examination, September 14, 1919, six months after the accident, revealed the same findings, except that the heart shadow was perceptibly smaller. Another examination made about three years later showed no change.

PRESENT REPORT

On December 12, 1949, at the age of ninety, the patient again entered the same hospital. A routine chest film (Fig. 1) revealed the same foreign body within the heart shadow. Five days after admittance the patient died of uremia, secondary to benign prostatic hypertrophy.

At postmortem there was noted "a small scar, 7 mm. in diameter, in the skin over the chest in a position 2 cm. to the left of the midline in the fourth interspace. The scar is slightly grayish in color and is consistent with a healed bullet wound.

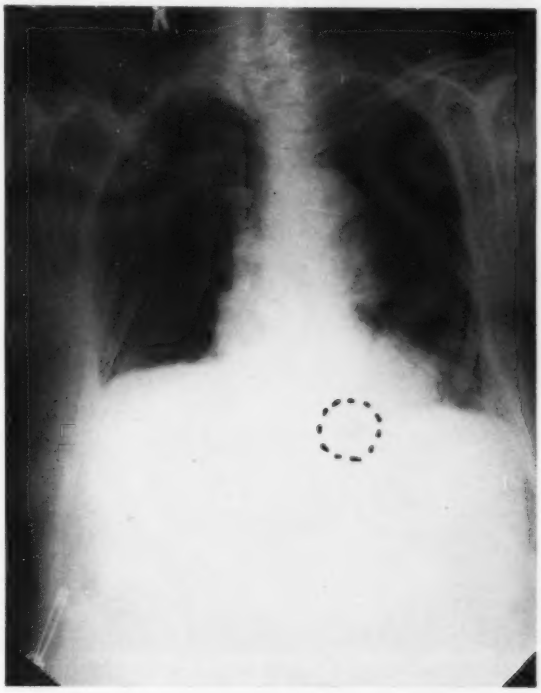

FIG. 1. Bullet noted in mid-portion of heart.

"The heart is slightly enlarged and weighs 450 grams. The pericardium is thin walled and smooth, and there are multiple fibrous adhesions, which bind the visceral and parietal pericardium together. On the anterolateral aspect of the right ventricle near the apex is a rounded scar.

"On section the scar involves also the endocardial surface and a rounded scar is noted in the mid-portion of the interventricular septum, where it lies contiguous to the right ventricle.

"Section through the interventricular septum reveals in its posterior half, approximately 1 cm. from the pericardial surface, a lead bullet slug which is pointed downward, posterior direction and measures 1.2 cm. in length and 7.6 mm. in diameter. Its forward end is rounded; posteriorly it presents a hollow depression. A small amount of fibrous tissue immediately surrounds the slug to encapsulate it. The heart chambers show only slight dilatation. The mitral valve measures 8.5 cm., tri-

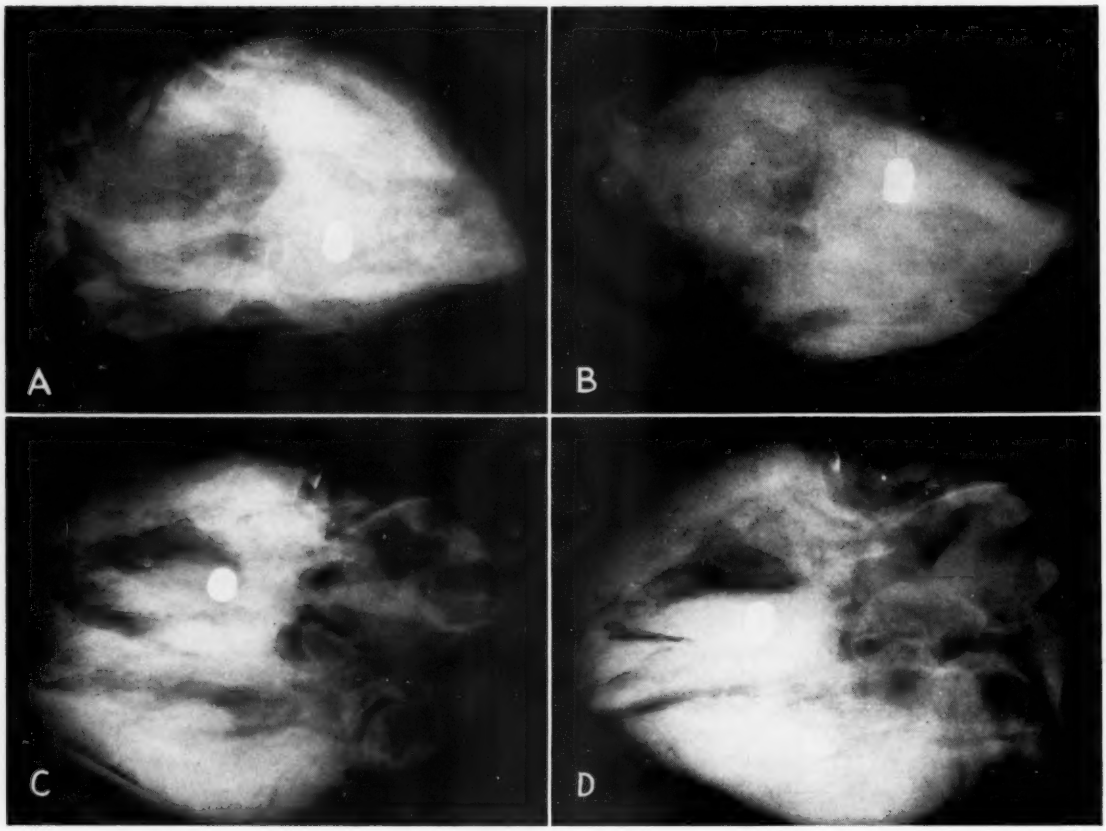

FIG. 2, *A*, *B*, *C* and *D*. Roentgenograms of heart after autopsy showing bullet.

cuspid 11 cm., pulmonic and aortic each 8 cm. in circumference. The coronaries are of large caliber showing only slight atherosclerosis. The aorta shows only minimal atherosclerosis in its abdominal portion.

"Microscopic examination revealed thin incomplete hyalin capsule containing a few fibrocytes adjacent to bullet. No pigment deposits. Underlying muscle normal."

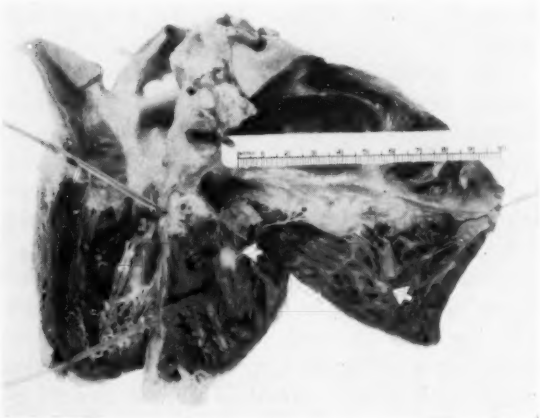

FIG. 3. Photograph of heart showing scar on interventricular septum.

Unfortunately, an electrocardiogram had not been made at any time. The bullet rested in an area which probably did not interfere with intraventricular conduction. The scar apparently did not induce heart failure, since the major coronary vessels were not involved. If this series of events occurred today, it is believed that conservative treatment would be advisable, rather than increasing the injury through surgery.

During the intervening years, the patient became slightly euphoric, possibly due to the realization of his frequent boast that he was the "only man alive with a bullet in his heart." He vowed that he would outlive the radiologist, twenty years his junior. He did.

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REGENERATION OF THE RESECTED DESCENDING ARTICULAR FACET OF THE FOURTH LUMBAR VERTEBRA

By MICHAEL BURMAN, M.D., *and* SAMUEL E. SINBERG, M.D.
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THE regeneration of the resected descending articular facet of the fourth lumbar vertebra is an unusual occurrence.

REPORT OF CASE

A man, aged twenty-five, lifted a piece of plywood, 10 feet long and 4 feet wide, in an awkward position on July 7, 1949. He had immediate sharp low back pain and felt "paralyzed." He was put to bed by his doctor for two and one-half weeks. He returned to his regular work on August 9 against advice. Prompt return of pain necessitated another hospital admission and bed rest for three more weeks.

On October 26, 1949, when we first saw him, he complained of toothache-like pain in the low back which did not radiate. He could not bend and found it most troublesome to put his shoes on. He avoided lifting. He was tall and thin. The lumbar spine was long. Flexion of the spine was slowly done to an angle of 120 degrees, the fingers reaching to 8–10 inches from the the floor. On this bending movement, the trunk inclined to the left and the lumbar spine became scoliotic to the right. Extension which was painful did not exceed 15 degrees. Lateral bending to each side was about 45 degrees. Left lateral bending provoked pain. The spinous process of the third lumbar vertebra was tender. The hip flexed to 110 degrees on the right straight leg raising test and to 120 degrees on the left. The prone knee flexion test was negative. There were no abnormal neurologic findings.

Roentgenograms of the lumbosacral spine taken on December 13, 1949 (Fig. 1) disclosed no evidence of fracture. The lumbosacral disc was narrowed and the lumbar spine scoliotic to the right. The oblique views revealed narrowing of the right apophyseal joint between L5 and S1 and widening of the right apophyseal joint between L4 and L5 and narrowing of its left mate.

The genesis of his illness, a lift against resistance, the physical findings, especially the obliquity of flexion of a long lumbar spine, and the roentgenographic findings pointed to a subluxation of the right lesser joint between L4 and L5 as the cause of his back disability. (This diagnosis has been made and operatively confirmed in other cases.)

Since he did not improve, the spine was explored on January 17, 1950, at the Hospital for Joint Diseases. The spinous process of L4 was tilted up and to the left. When this process was seized and rocked with a heavy Kocher clamp, both before and after the division of the interspinous ligaments, there was no passive movement of this vertebra. The same observation was made when the spinous process of L5 was rocked. The apophyseal joints between L4 and L5 were now exposed. The capsule of each joint was thin and adherent. The right small joint had been sprung open so that the joint space, easily 3/8 inch wide, admitted a thick periosteal elevator (Fig. 2). The left small joint was narrowed and did not admit the elevator. The left joint had moved to the frontal plane. The active moving element of the right small joint the descending facet of L4, had moved forwardly and to the left to cover the ascending facet of L5. The position of these joints indicated that the fourth lumbar vertebra had been rotated to the right and forward.

Bilateral resection of the articular facets is inadvisable because the solution of continuity of the posterior arch is endangered. To all intents, the left small joint was fixed. The right descending facet of L4 was resected. The ascending facet of the joint, rotated also into a semifrontal plane, was then exposed and much of this facet was also resected. The joint cartilage was still smooth but gray and opaque. The intervertebral foramen was not explored since there were no neuritic symptoms.

The patient made a good postoperative recovery. A roentgenogram taken on February 16, 1950 (Fig. 3) showed only a partial resection of the descending facet of L4. A plaster jacket was applied on January 23, 1950, and this was replaced by a strong corset on February 24, 1950. He was given physical therapy until May

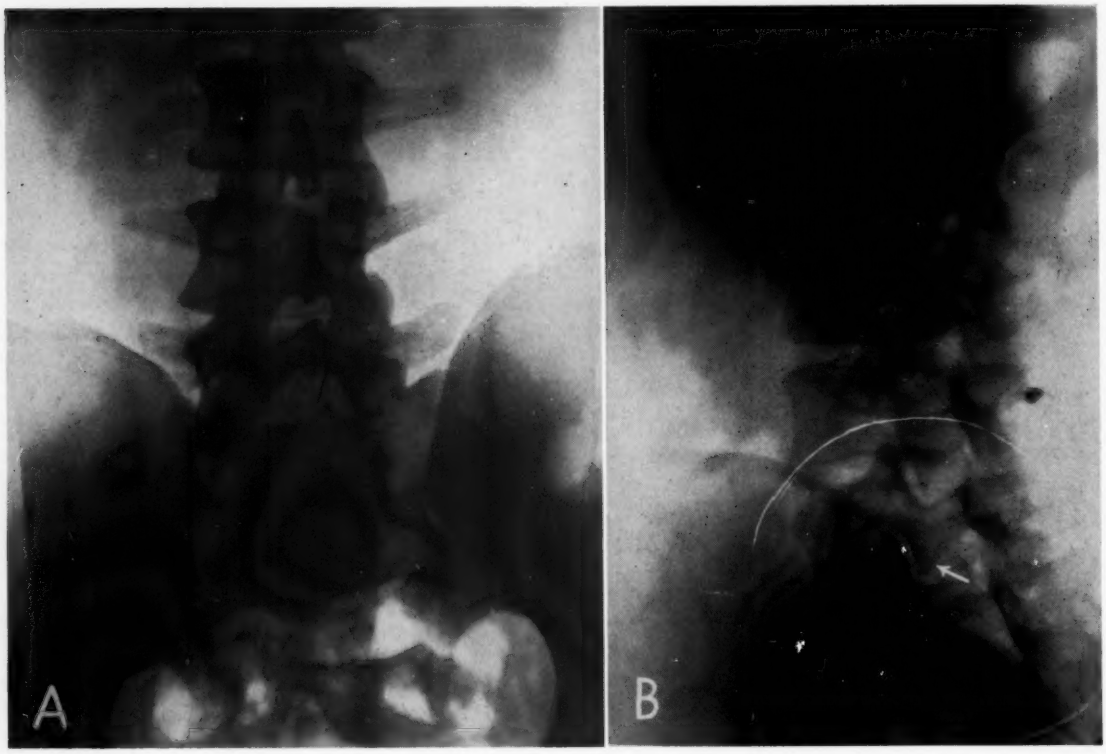

FIG. 1. The anteroposterior (*A*) and right oblique (*B*) roentgenograms of December 12, 1949. The apophyseal joint between L4 and L5 is anteriorly tilted and its joint space broadened in the oblique view. The upward tilt of the spinous process of L4 and the rotation of the vertebra to the right is shown in the anteroposterior view.

8, 1950, when treatment was discontinued. He now enrolled in a school to learn body and fender repair of automobiles, a form of work demanding repeated bending and some measure of lifting. He had no pain on June 9. In fact, the back pain which he had always felt disappeared immediately after the operation.

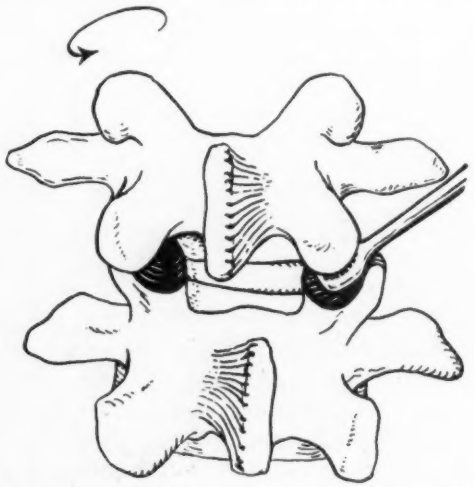

FIG. 2. A sketch to illustrate the operative findings. A periosteal elevator is placed in the right apophyseal joint between L4 and L5.

Motions of the spine were slightly restricted. Flexion reached 90 degrees, extension 60 degrees, right lateral bending 60 degrees and left lateral bending 50 degrees. Straight leg raising was allowed to 95 degrees on each side. There were no tender areas. On August 11, he again had pain lasting two days. Tenderness was now present over the spinous process of L3 and there was moderate restriction of motions of the back. The leg tests were negative. This sprain between L3 and L4 followed the repeated bending demanded by his work. Physical therapy was again given until October 20, 1950, when the back was essentially normal.

A year later, on October 3, 1951, he had no complaints. He had been working fairly regularly since March 15, 1951, as a stock clerk. The roentgenogram (Fig. 4) revealed regeneration of the resected descending facet of L4.

Comment. It is unnecessary to enter into the mechanics of the lift against resistance which subluxates the apophyseal joints of the spine. Let it suffice to say that we believe this to be the common denominator of all low back sprain, a more dramatic expression of which is the sometimes associated herniation of the intervertebral disc at the same or different level. It is axiomatic that a herniated disc cannot exist unless there be strain or subluxation of the apophyseal joints, the most common site of which lies between L_4 and L_5. The converse is not true, for, as this and other cases prove, there can be apophyseal joint subluxation without disc herniation. The displacement of one point means direct displacement of its mate by break of their paired joint movement. Since each vertebra joins in joints with the vertebra above and the vertebra below it, there is at its least a disturbance of the motions of two pairs of joints, the greatest expression of which is found at the site of primary luxation.

The study of a roentgenogram of the lumbosacral spine cannot reveal to us if the patient has a backache. The four routine views of the lumbosacral spine show the position of the facets and the widths of their joint spaces. It is difficult roentgenologically to decide that a given small joint is subluxated. Slight variations in the oblique positioning of the patient, or in the position of the roentgen tube, are factors in producing simulated luxations. The association of the history, the clinical findings and the roentgenographic findings, the latter compared in the mind's eye with the presumed normal, a variable normal to be sure, is needed to establish a diagnosis of apophyseal joint luxation. The operative findings are irrefutable. The normal joint does not admit the periosteal elevator. The normal joint shows matching congruence of the moving descending facet and the relatively stable ascending facet.

Fig. 3. Right oblique roentgenogram taken on February 15, 1950, to show the resection of the distal half of the descending facet of L_4.

Fig. 4. The right oblique roentgenogram of October 3, 1951, showing regeneration of the resected facet.

The roentgenogram does not reveal fully the extent of resection of a facet, except its total resection. Thus the resection of the ascending facet is not shown in the immediate postoperative roentgenogram or in the later roentgenograms. The study of the three oblique roentgenograms, reproduced here, indicated that an unusual occurrence took place—the regeneration of the descending articular facet of the fourth lumbar vertebra.

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ENDOMETRIAL BIOPSY AS A STANDARD DIAGNOSTIC TECHNIQUE*

A REVIEW OF 445 CASES

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ENDOMETRIAL biopsy as a valuable diagnostic procedure in malignancies of the uterine corpus has been given only reference attention in the literature and has been consistently discouraged because of its presumed inadequacies. In our experience, where negative microscopic reports are followed by a dilatation and curettage to confirm or invalidate the findings, sufficient evidence has been accumulated to warrant the establishment of endometrial biopsies as a standard diagnostic technique for the detection of endometrial cancer.

An endeavor has been made to facilitate the diagnosis of endometrial carcinoma and to evaluate the accuracy of the endometrial biopsy as a diagnostic procedure. Over the past five years endometrial biopsies have been done on 130 patients with the complaint of irregular bleeding. These were done at the initial visit of the patient to the private office of one of the authors, (J.A.W.). Moreover, another 315 patients were biopsied at the M.D. Anderson Hospital for Cancer Research. Although there have been 2 patients, aged thirty-one and thirty-two years, with cancer of the uterine corpus, thirty-five has arbitrarily been selected as the age beyond which endometrial carcinoma should be ruled out in the differential diagnosis. It has been estimated that 25 per cent of adenocarcinomas of the uterine corpus originate prior to the menopause.[1]

With one exception, where insufficient tissue for adequate histopathological examination has been obtained on endometrial biopsy, cancer has not been demonstrated later either by curettage or hysterectomy. Therefore, when an endometrial cavity is explored with care, and no tissue can be obtained, one might be reasonably certain that a malignant change in the uterine cavity has been ruled out. On the other hand, a positive diagnosis from conventional hematoxylin-eosin stain on biopsied material can be returned with in twenty-four hours and allows for the prompt admission of the patient to the hospital with an established diagnosis and plan of therapy. This is far more reliable than an attempt to carry out a frozen section study of curettings and then the insertion of radium, if a positive diagnosis of malignancy is rendered. To reiterate, however, a negative endometrial report is never accepted as sufficient evidence to rule out malignant disease, but always the importance is stressed of a dilatation and curettage under anesthesia.

If the patient is symptom free, except for spotting or more profuse irregular bleeding, it is sometimes difficult to persuade her that the condition may be serious enough to justify the performance of a curettage. It is interesting to note that of the private negative endometrial biopsy cases on whom a curettement was advised, 36 per cent did not follow through with recommended treatment for reasons of expense, inconvenience or procrastination. Of these 36 per cent, malignancy has at least tentatively been ruled out and to date there has been no evidence of cancer in any who have been followed.

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The endometrial biopsy affords a means of early diagnosis of cancer. As in biopsies in any part of the body, it is not an absolute criterion, but in this series, when adequately performed, it has furnished evidence to establish the diagnosis of cancer of the endometrium comparable to other diagnostic procedures.

Of the 445 biopsies in this study, confirmation by curettage or hysterectomy revealed only 3 missed cancers. Cancer was present in 95 individuals; 15 of the cancers were detected in the office practice, 13 of which were found by endometrial biopsy alone. Of the hospital patients, 80 had cancer of the endometrium, in 79 of whom the endometrial biopsy was the only diagnostic measure (Fig. 1).

The 3 patients, in whom the malignant neoplasm was not diagnosed by endometrial biopsy, deserve more detailed analysis.

Mrs. M. F., aged forty-eight, with a nodular uterus the size of an eight to ten weeks pregnancy, had a negative endometrial biopsy prior to hospital admission. A diagnostic curettage was performed and radium was available when she was taken to surgery. The curettage did not reveal sufficient tissue for histopathological examination, and a total abdominal hysterectomy was forthwith carried out with the mistaken clinical impression of bleeding, due to leiomyomas.

Pathological examination revealed in the fundus of the uterus a polyp about 1 cm. in diameter at the base, and approximately 0.8 cm. high. Microscopic examination of this polyp revealed the presence of a large broad-based growth arising from the myometrium and made up of a very anaplastic adenocarcinoma. Next to the base of the polyp was a small area of endometrium with benign appearing epithelium and surrounded by considerable fibrinous exudate "as though recently curetted," according to the pathologist's note. The deepest penetration in the myometrium was about 0.3 cm. from the endometrium.

ENDOMETRIAL BIOPSY IN 445 WOMEN WITH BLEEDING AFTER AGE 35 YEARS

	CANCER PRESENT	CANCER MISSED
PRIVATE	15	2
ANDERSON HOSPITAL	80	1
TOTAL	95	3

FIG. 1

The lesson learned from this experience served to emphasize the necessity of exploring the uterus with some type of forceps at the time of curettage in order that such elusive polypi may not be overlooked.

The second patient, Mrs. A. J., aged forty-seven, had a negative endometrial biopsy in the presence of bleeding which was presumed to be due to a myomatous uterus. A total abdominal hysterectomy and bilateral salpingo-oophorectomy was done without a preliminary diagnostic curettage. On opening the specimen, a thick hyperplastic polypoid endometrium was found, measuring about 0.5 cm. in thickness. The numerous small polypoid projections were hemorrhagic at the distal ends. Microscopically, the basal glands were found to be hyperplastic, but superficially, there was a large mass of gland tissue which stained much more deeply and even appeared somewhat demarcated from the basal layer. There was a zone of benign hyperplastic endometrium between the myometrium and the tumor cells in all areas secured for study by serial section. This patient's endometrial biopsy had been difficult to interpret because of the large amount of blood present.

However, in retrospect, this emphasizes that it is imperative to do a diagnostic curettage in the presence of a negative endometrial biopsy where adenocarcinoma of the endometrium is to be excluded.

Patient A. S. had a curettage by the referring physician three weeks before hospital admission and insufficient tissue was obtained in the clinic for adequate histopathological examination.

The technique of endometrial biopsy is the same as that utilized in the study of the endometrium for any other type of irregular uterine bleeding in all age groups. The patient is placed in the lithotomy position and a careful bimanual examination is made. No anesthesia is employed,

and ordinarily there is little discomfort. The internal os is almost invariably patent where there is neoplasia in the endometrial cavity. This in itself is a useful diagnostic sign. A bivalve speculum is introduced and the cervix is cleansed of all discharge. No antiseptic is used, but care is taken to insert the instrument directly through the external os. A sterile uterine probe is inserted first to determine the length and the direction of the uterine cavity and to verify the impressions gained on bimanual examination. The preferable curette has been described by Randall[2] and is known by his name (Fig. 2, 3 and 4). Suction on this instrument is not necessary. The fenestrated surface of the instrument is applied firmly to the anterior wall and pulled down with a swift stroke and pushed back into the uterine acvity and turned first to one side and then the other until the uterus is thoroughly curetted. The curette is usually not removed until the entire cavity has been explored. If the uterus is freely mobile, a tenaculum may be used to steady the cervix. Traction is avoided because it precipitates more pain on the sensitive visceral peritoneum. The whole procedure causes some discomfort to the patient, but in general there is a minimal amount of pain.

In this series there have been no complications, and although the probability of perforation in the presence of a malignancy of the uterine corpus has been emphasized

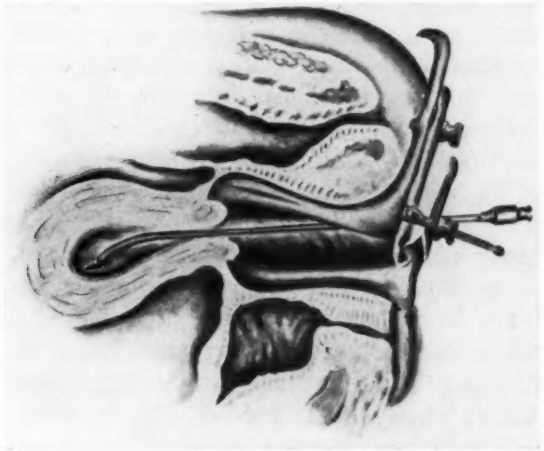

Fig. 2

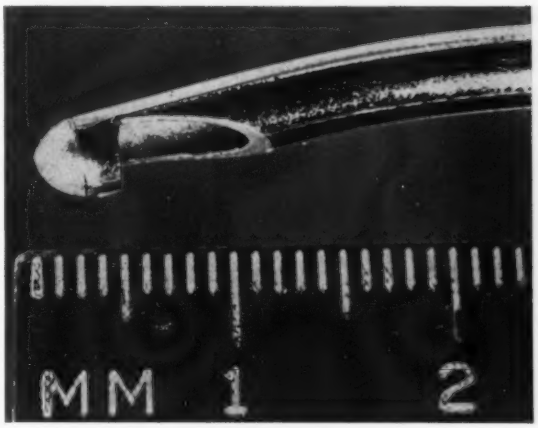

Fig. 3. Randall curette.

in the literature, this disaster has been avoided. If, on introducing the sound, a pyometra is encountered, sufficient tissue cannot be obtained in most instances. However, several sweeps around the uterine cavity have been made without hesitancy, and occasionally with recovery of sufficient tissue for a diagnostic histopathological examination. There have been no infections in this series and no cause to suspect dissemination of tumor.

There are insurmountable handicaps in the women who tend to develop endometrial neoplasia and certain impressions stay with the clinician in diagnosing cancer of the endometrium. Many of these women are obese, hypertensive, often diabetic, and give a history of menstrual arrhythemia and infertility. One explanation frequently offered is that there is an estrogen corpus luteum imbalance associated with this disease. Lack of ovulation leads to a lessened gravidity and tends to produce endometrial hyperplasia which is recognized as a frequent precursor of endometrial cancer. Gynecologists should therefore emphasize to infertile patients the significance of routine pelvic examinations. They should particularly be viewed with suspicion if they are of an endocrinopathic habitus.

In an effort to confirm or refute these impressions the histories of 114 endometrial cancer patients have been analyzed. Of these, 93 cases are from the records of the

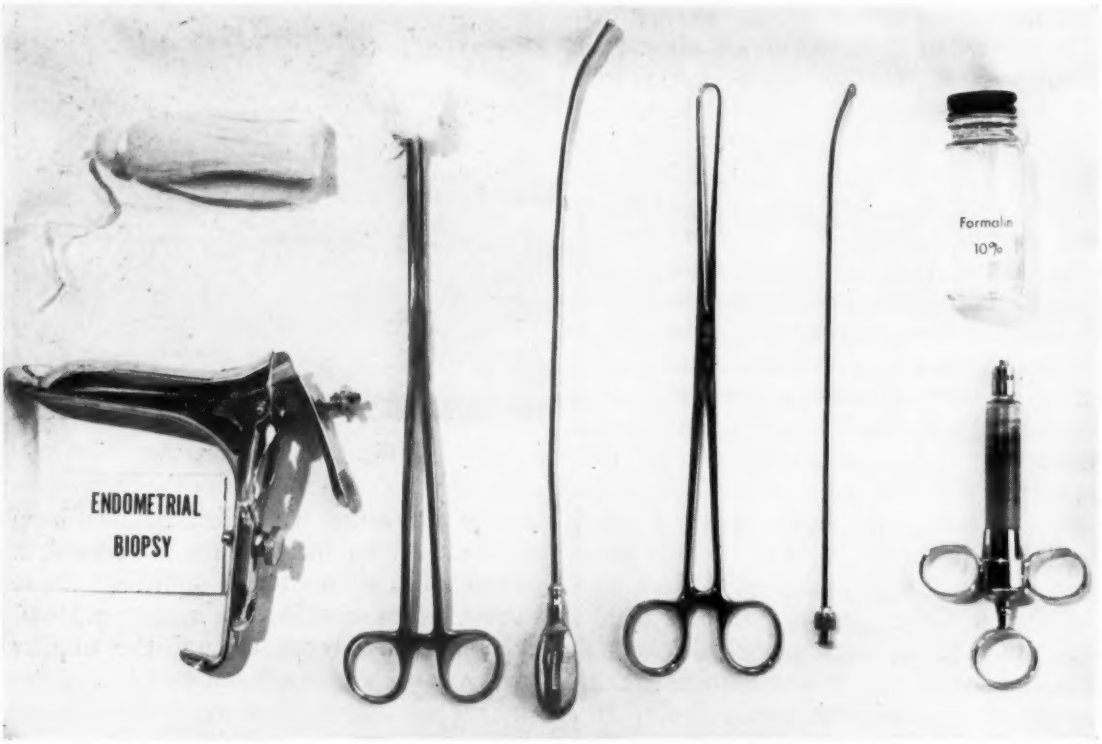

FIG. 4. Instruments necessary for endometrial biopsy.

M. D. Anderson Hospital for Cancer Research, and 21 from a general gynecological practice. In this series 23 per cent of the women weighed in excess of 200 pounds; 65 per cent of the women were under 65 inches in height and, of these, 70 per cent were more than 20 per cent overweight. Thirty per cent were 65 inches or over in height and, of these, only 23 per cent were overweight (in excess of 20 per cent). There was hypertensive heart disease in 59.6 per cent, 7 per cent were diabetic; the average age was 52.7 years, and the average age at menopause was 49.7 years (Fig. 5).

114 ENDOMETRIAL CANCER CASES

23%	WEIGHED IN EXCESS 200 LBS.
70%	OF WOMEN UNDER 5' 5" IN HEIGHT WERE MORE THAN 20% OVERWEIGHT
59.6%	HYPERTENSIVE HEART DISEASE
7%	WERE DIABETIC
57.2	YEARS AVERAGE AGE
49.7	YEARS AVERAGE AGE AT MENOPAUSE

FIG. 5

There was a great difference in the findings in the number of children in the two series. The hospital series of 93 showed 15 with no children and 7 women with only 1 child, or 23.6 per cent with absolute or a relative infertility. For comparison, 52.6 per cent was the figure found in the office group, with 5 having no children and 6 having only 1 child. This is a total of 11 out of 21 with relative infertility. The other women averaged 5.5 children in the clinic group and 4.0 children in the office group. In each series there was 1 unmarried woman. In the hospital series there were 71 white women and 22 Negro patients, while in the office group, all 21 patients were white. The demonstrated difference brings to mind several questions. Is it the variance in the size of the series, or is it the economic,

intellectual or racial status of the patients?

Endometrial biopsy has proved of value in planning the treatment in carcinoma of the endometrium. It is extremely important to localize the process in outlining the therapeutic plan. Experience has shown, for example, that primary adenocarcinoma of the cervix is a relatively rare neoplasm. It is much more frequent to find that a so-called primary carcinoma of the cervix is actually endometrial carcinoma which has extended downward to the cervix. Some authors indeed prefer to classify these lesions in a separate category as "carcinomas of the body and cervix," but, nevertheless, it is apparent that one must treat the lesion in the cervix as well as in the fundus. Endometrial biopsy has proved of significant benefit in determining the presence or absence of adenocarcinoma in the fundus in such instances. It is routine where adenocarcinoma is reported in the cervix to do an endometrial biopsy in order that the presence or absence of neoplastic change above the internal os can be demonstrated. Therefore, in planning the treatment, the cervix can be treated with cancerocidal irradiation, but one can also make sure that the fundus has adequate therapy. Failure to prove the presence of carcinoma in the endometrium has led to a misconception about the so-called radioresistance of adenocarcinoma in the cervix. Actually, failure does not represent a recurrent lesion in many instances, nor a radioresistant lesion, but is persistent disease because of inadequate dosage above the level of the internal os

Endometrial biopsy is frequently difficult in combined adenocarcinoma of the cervix and fundus because the disease has been long neglected. Distortion of the endocervical canal may, therefore, make diagnostic curettage under anesthesia imperative.

The Heyman packing technique of irradiation is employed and a calculated total of 4,800 gamma roentgens (3,000 –4,000 mg. hr.) is delivered to the body of the uterus for a distance of 2 cm. beneath

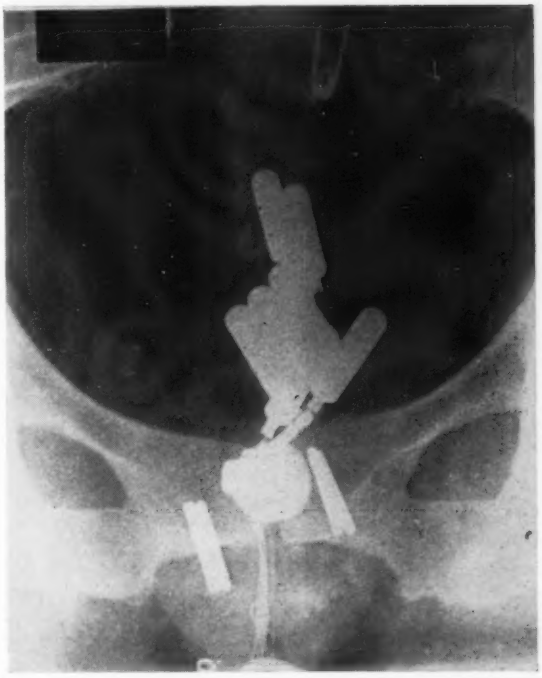

Fig. 6

the endometrium. This dosage is administered in two sessions, three weeks apart. Cognizance of the possibility of lymphatic metastasis of the tumor through the superficial lymphatic vessels beneath the endometrium to the cervix or vaginal vault or under the urethra from venous emboli[3] makes adequate irradiation of the vaginal tube imperative. Proper irradiation to the vagina is the most valid argument for preoperative radium treatment in carcinoma of the endometrium (Fig. 6). In addition to the intrauterine radium therapy, 3,000 gamma r is administered to the vaginal mucosa by means of Manchester ovoids placed in each lateral fornix. The application to the vault of the vagina is done when the uterus is packed with multiple sources at the time of the first treatment. The long axis of the radium sources is perpendicular to the long axis of the vagina. At the time of the second packing of the uterus with multiple sources, a vaginal cylinder with two or three linear sources of radium, depending upon the length of the vagina, is employed to administer another 3,000

FIG. 7

gamma r to the vaginal mucosa (Fig. 7). A total abdominal hysterectomy and bilateral salpingo-oophorectomy is performed four weeks following the second radium treatment. No particular effort has been made to remove the upper third of the vaginal vault because it is felt that the radium in the vagina offers sufficient prophylaxis in this area.

The advanced age of the patient, the frequency of obesity, hypertension, and diabetes, as well as other intercurrent diseases, will usually preclude radical surgery. Lymph node dissection does not seem indicated except in a few well selected instances, and should not be regarded as advisable as a routine measure. Radium is preferable to roentgen therapy for preoperative use because it should deliver the greater dose to the tumor in the uterus and to the potential microscopic foci of tumor cells in the vagina. It is obvious that roentgen therapy of significant proportion would usually be directed to the parametrial extention of tumor, and adequate dosage to the lymph nodes is highly improbable in the typically obese patient with endometrial carcinoma (Fig. 8).

Eleven patients in the private group and 15 from the M. D. Anderson Hospital series have been analyzed to make a total of 26 patients who have been given what is considered adequate therapy throughout (Heyman's packing technique followed by hysterectomy). There was no tumor demonstrated in the uterus after hysterectomy in 17, or 65 per cent. There were marked changes in the tumor microscopically in 6, or 23 per cent, and there was residual tumor in 3, or 12 per cent. Emphasis is laid on the need for an early diagnosis in order that such results can be obtained, and the endometrial biopsy offers a means by which the diagnosis can be more promptly established.

A sizable series of cases with standard treatment is difficult to accumulate because of obesity and intercurrent diseases, associated with the fifth and sixth decades of life, which are irreversible. However, such handicaps can be favorably influenced by an earlier diagnosis and endometrial biopsy offers a tangible means of improving the prognosis.

To further point out the value of the endometrial biopsy as a diagnostic agent, it seems worthy to mention that of the 21 private office endometrial carcinomas, 76 per cent, or 16 cases, were early and pre-

26 PATIENTS WITH "ADEQUATE" PRE-OPERATIVE IRRADIATION

17 — (65%) SHOWED NO TUMOR IN HYSTERECTOMIZED SPECIMEN

6 — (23%) SHOWED MARKED CHANGES MICROSCOPICALLY

3 — (12%) SHOWED RESIDUAL TUMOR

FIG. 8

viously untreated, yet in the hospital series of 93 cases, only 24 per cent, or 22 cases, were in the early stage. All the hospital patients were referred by physicians throughout the state and predominantly from rural communities and had been subjected to a wide variation of treatment before their admission.

SUMMARY

The prognosis of endometrial carcinoma with early diagnosis has been considerably improved through the cooperation of radiotherapists and the surgeons. Thus, it is the obligation of the clinician to improve the means of making an early diagnosis by a method available to both rural and urban physicians in patients having irregular bleeding. Endometrial biopsy on the initial visit to the physicians office should become a standard technique; a negative microscopic finding should be followed by a diagnostic curettage. This is the means by which earlier diagnosis may be established. Earlier treatment affords a better outlook to a greater number of women who might otherwise pass into a late stage with the attending poor prognosis.

CONCLUSIONS

1. Endometrial biopsy should be utilized as a diagnostic technique in malignancies of the uterine corpus. A study has been made on 445 women with irregular uterine bleeding beyond thirty-five years of age.

2. Adenocarcinoma of the endometrium was present in 95 of these individuals and the cancer was diagnosed by endometrial biopsy alone in 92 cases.

3. Endometrial biopsy offers a means of establishing an earlier diagnosis to counterbalance other unalterable handicaps encountered, as a rule, in women who develop adenocarcinoma of the endometrium.

4. Endometrial biopsy is useful in localizing the tumor and is a means by which combined adenocarcinoma of the uterine body and cervix can be differentiated from true primary adenocarcinoma of the cervix.

5. The plan of treatment can be altered accordingly.

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FAST CAMERAS FOR ALL-PURPOSE PHOTOFLUOROGRAPHY*†

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IN JANUARY, 1948, there appeared in the AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY my paper[1] on "Bernhardt Schmidt," which was to be the first of a series of five papers on reflector cameras. Papers No. II, III and IV, written respectively by George S. Monk,[2] Russell H. Morgan *et al.*,[3] and L. G. Henyey and J. L. Greenstein,[4] followed on schedule in the February, March and April numbers of Volume 59; but this present paper, No. V, dealing with reflector cameras employing the Henyey and Greenstein optical systems, which we hoped would appear in May, 1948, has been delayed for more than four years. The delay was caused largely by difficulty in obtaining the 90 pound block of dense barium crown optical glass required for one of the elements in the so-called "doublet" of the 70 mm. camera and, to a lesser extent, by the serious temporary illness of the principal lens maker and later the illness and subsequent death of the precision machinist most responsible for the work on the nonoptical portions of the camera.

PRELIMINARY 35 MM. REFLECTOR

In the early American models of 35 mm. chest microfilm apparatus the lenses were not specially designed but, instead, merely adapted from other fields of photography. The best of them had speeds as great as f/1.5 but at the necessarily short working distance of 0.9 meter their resolving power was poor. Russell Morgan and I were impressed with the desirability of employing lenses that were faster and particularly that had much better resolving power, and in 1944 we suggested replacing refractors by specially designed reflectors of the general type of those invented by Schmidt in 1930 for stellar photography. While the Office of Scientific Research and Development was considering our suggestion, the f/1.5 Ektar lens became available, providing all the speed and resolving power that were needed for microfilming the chest, but it was recognized that even more speed would be needed for microfilming of heavier body parts and so in July, 1944, the Office of Scientific Research and Development authorized us to try our hand at reflector systems. Our erstwhile colleagues, L. G. Henyey and J. L. Greenstein, designed a 35 mm. optical system for us. Since the flint and crown lenses used in this instrument had diameters of only $3\frac{1}{2}$ inches, they could be constructed from optical blanks immediately available from glass manufacturers and Mr. Fred Pearson ground the mirror and lenses in the Optical Shop of The University of Chicago's Yerkes Observatory, completing his work early in 1945. By that time, however, Dr. Morgan had become increasingly engaged with work for the United States Public Health Service in Washington and I with the continuation of our joint phototiming project at The University of Chicago and we were not able to get on with construction of our reflector camera.

With the close of World War II and the establishment of the Office of Naval Research, we applied to that agency for funds with which to attempt to bring all body parts within the range of photofluorography. We planned two separate approaches and grants were made for both. One plan was to complete the 35 mm. reflector camera and use it to photograph conventional fluoroscopic screens. The other was to electroni-

* Supported by Grant from the Office of Naval Research.

† Presented at the Fifty-third Annual Meeting, American Roentgen Ray Society, Houston, Texas, Sept. 23–26, 1952.

cally amplify the fluoroscopic image to the point where it could be photographed by ordinary cameras. The Office of Naval Research grant was received in May, 1946, and by September of that year our 35 mm. instrument was almost ready to operate.

About the time when we began to be interested in reflector cameras, Dr. Johannes Holm in Copenhagen independently developed a similar interest and began working with a Schmidt system that was constructed for him by the Danish optical designer, Helm. Dr. Herman E. Hilleboe, at that time Chief of the Tuberculosis Control Division of the United States Public Health Service, saw the 35 mm. Helm reflector in operation when he visited Dr. Holm's laboratory in 1946 and arranged for the importation of a 35 mm. and later a 70 mm. instrument. Our own 35 mm. camera went into operation in November, 1946. It proved to have excellent resolving power but was only about twice as fast as the f/1.5 70 mm. Ektar and hence not fast enough for microfilming heavy body parts. Furthermore, it was clear that 35 mm. film was not large enough for such work.

CONSTRUCTING THE 70 MM. REFLECTOR

In November, 1946, Greenstein and Henyey were developing the design of a 70 mm. optical system having a theoretical speed of approximately f/0.60 and we were attempting to deform 70 mm. film to a 4 inch spherical radius which would have been ideal for the new system. Eventually we had to settle for a spherical radius of 4.98 but that extra inch of film radius unfortunately required a geometric increase in the size of the lenses and mirror so that in the final design the blanks for the two lens elements had diameters of nearly 15 inches and weighed approximately 90 pounds each. By February, 1947, the Office of Naval Research had agreed to finance a 70 mm. camera and by April the optical design was complete and the glass had been ordered from a West Coast company which promised delivery in five months.

OBTAINING THE OPTICAL GLASS

By June, 1947, it seemed probable that the California glass people were in over their depth and ONR allowed us to seek alternative sources, even at the risk of duplicate delivery. The Bausch and Lomb Company, which makes large quantities of excellent optical glass, are not set up to produce blanks as large as these and it would have required much time and considerable money to tool up for such large pieces in the same way that they are tooled for microscope lenses, spectacle lenses, camera lenses, etc. They would have preferred not to undertake our job at all but as a courtesy to the Navy and the University they accepted our order late in June, 1947, without firm commitment as to delivery date. Eleven months later (May, 1948) they had produced an excellent flint glass blank for us but, in spite of two years of hard work that was expensive and extremely inconvenient for them, they were not able to press and anneal an acceptable blank for the crown glass element.

The Pyrex glass for our 24 inch mirror had presented no difficulties whatever to the Corning Glass Company, which some years earlier had produced the 200 inch mirror for Palomar, but it was not until early 1949 when war-time restrictions were beginning to be relaxed that we learned that during the war Corning had built an optical glass plant of unique design. In mid-February, 1949, while the sixth attempt at a crown glass blank was still in the annealing oven at Rochester, we placed an order with the Corning Glass Company for a similar piece of crown glass and received it seven months later. By March, 1950, in spite of Fred Pearson's serious illness, the element made from Bausch and Lomb flint glass and that from Corning crown glass were completed and at last we were free to proceed with construction of the heavy parts of the camera.

BUILDING THE CAMERA

The great delay in obtaining the optical glass had many unfortunate connotations.

Until both elements were in hand and their actual indices known, the final design of the optical system could not be established and neither element could be ground and, until the grinding was complete, the lens cells and other cast iron parts of the camera could not be constructed. In a small experimental shop like ours the construction of a large instrument taxes facilities to the utmost. We would clear the shop program for the camera job, then turn back to other work, then get ready again for the camera, repeating the process over and over for two years as our hopes of receiving the optical glass rose and fell. As a result, shop costs rose sharply and the Office of Naval Research, which operates on an annual budget, was embarrassed and inconvenienced because our project lagged so far behind schedule.

Throughout the period of the lens grinding and continuing through the construction and assembling of the camera we have had frequent expert advice and assistance from Professor W. Albert Hiltner of the Yerkes Observatory. However, even with that help we have not been able to proceed as rapidly as expected, first because of the serious and protracted illness and eventual death of Mr. Stanley Doles, our chief machinist, and, second, because of the necessity of diverting eight months of shop time to other pressing work that had previously been put aside to make way for the camera. By June, 1951, the 70 mm. camera was in operating condition with the optical system columnated and focused but at that point the work had to be put aside until the Spring of 1952.

Now, finally, in the Summer of 1952 the camera has been installed and given clinical trials and after certain changes have been made in the film-moving mechanism it will be put into regular clinical service. Already there is reason to believe that the instrument will be useful for cerebral and cardiac angiography and for trunk and extremity surveys as well as for gastrointestinal work, and it is for that reason that I have changed the title of my paper slightly from the one that appears in the program.

OPTICAL SYSTEM

Figure 1, which illustrates the optical system, is drawn with the distance between fluorescent screen and film greatly fore-

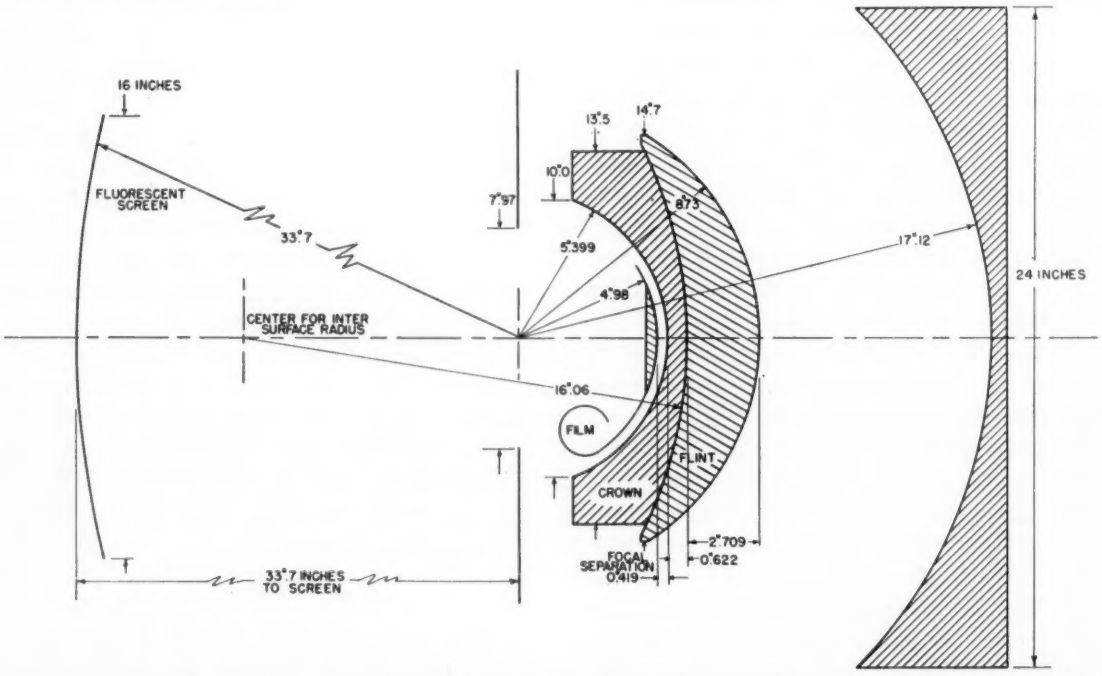

FIG. 1. Henyey and Greenstein optical system for 70 mm. reflector camera.

shortened and with the system laid on its side in order that the artist might make the drawing as large as possible so that it would show up better in the lantern slide. Actually the mirror lies parallel with the floor and the spherical fluorescent screen is approximately 51 inches above it. The screen, a sheet aluminum spinning, approximately 24 inches in diameter, was given its fluorescent coating by the Patterson Division of the DuPont Company and the 70 mm. film, green sensitive emulsion on unperforated base, 0.0095 inch thick, is put up for us by the Eastman Kodak Company in 50 foot lengths on daylight loading spools. The flint glass lens rests on thin paper pads in a gray iron lens cell and the crown lens floats on a capillary bed of cedar oil in the concavity of the flint. A rubber "O" ring encircling the crown and pressed down against the flint acts as an oil seal. The concave surface of the crown and the convex surface of the flint have not yet been given molecular coatings. If eventually they can be coated, some gain in speed may be expected.

Columnation is done by maneuvers well known to telescope makers and for this work provisions are made for shifting and tilting the mirror and shifting the lens cell relative to the film, mirror and screen. During exposure the film is stretched tightly and smoothly over an optically ground spherical surface that has a radius of 4.98 inches, a surface which we speak of as the "button." Focusing is accomplished by raising and lowering the button relative to the lenses, this being done by a screw which moves the button 0.025 inch for each complete turn. When the system is in focus, the surface of the film lies approximately 0.419 inch above the concave surface of the crown glass lens and movement of the button by as little as 0.003 inch produces demonstrable improvement or deterioration in the sharpness of the image.

HOOD AND BODY OF CAMERA

Figure 2 shows the assembled camera. It stands $65\frac{1}{2}$ inches high, has an over-all diameter of 39 inches, and with its lenses and mirrors in place weighs 1,360 pounds. At the top is seen the spherical aluminum spinning that carries the fluorescent screen on its concave inner surface. At the observer's right is the film-moving mechanism and above it near the base of the "hood" is seen a short brass sleeve or nipple which receives the detector tube of the phototimer.

Fig. 2. General view of reflector camera. The 24 inch front-surfaced mirror lies below, parallel with the floor, its concave surface directed upward. The flint element lies in the narrow throat above the mirror and the crown element floats in cedar oil in the concave surface of the flint. The film-moving mechanism is seen at the right, the concave fluoroscopic screen at the top.

FILM-MOVING MECHANISM

Figure 3 shows this mechanism cranked partly out of the slot which runs down through the base of the hood and the side of the throat. We avoid this maneuver as far as possible because it admits dust to the interior of the camera, employ it only when the leader of the film becomes broken or fouled in the mechanism or lost in careless

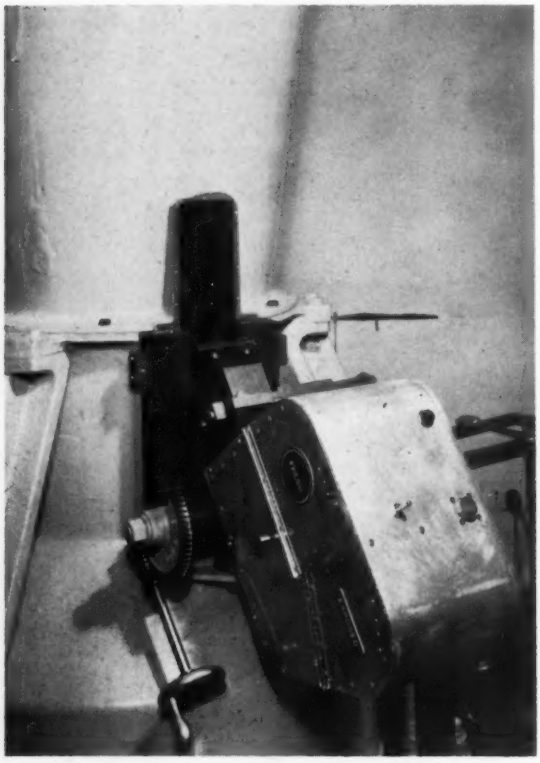

FIG. 3. Film-moving mechanism cranked partly out of the throat of the camera. The mechanism has to be cranked out of the throat only when the film leader has been damaged.

reloading. Hinged doors in the side of the housing allow removing lengths of exposed film or inserting spools of fresh film.

In Figure 4 the entire mechanism has been removed from the camera and the side taken off to reveal the metering roll, supply and take-up spools, etc. The take-up spool is at the observer's upper right, the supply spool at the upper left, and the rubber-covered metering roll at the lower right. Extending to the left is the "blade" which terminates in the button. It is in fact a light-tight duct which conducts the film across the flat rim of the crown lens down close to its concavity and thence to the focal surface on the button. The solenoid hanging below the aluminum housing operates the clutch and in a later model will be located in a separate power unit.

In Figure 5, which shows the other side of the film-moving mechanism, the lower plate of the film duct has been removed to reveal the sturdy steel lever that presses button and film firmly against the "frame" in that half of the film-moving cycle during which the exposure is being made and moves film and button back away from the frame in that half cycle during which the film is being advanced. The drive shaft protrudes from the side of the aluminum housing and below it and to the right can be seen a massive metal block which constitutes half of the hinge that attaches the housing to the body of the camera.

In Figure 6 the film-moving mechanism has been cranked back into operating position and the dust-proof plate replaced on the slot. The temporary motor drive that is seen attached to the drive shaft allows either single exposures or a series at intervals of approximately two seconds. This slow and fixed speed has been adequate for the experimental work but the power unit described below will allow varying the rate of film transport over a range of 1 per second to 6 per second.

POWER UNIT

We are now designing and presently will construct a separate power unit that will connect to the drive shaft through a flexible coupling. It will contain a driving motor, a variable speed reducer, a magnetic clutch, certain of the microswitches and relays

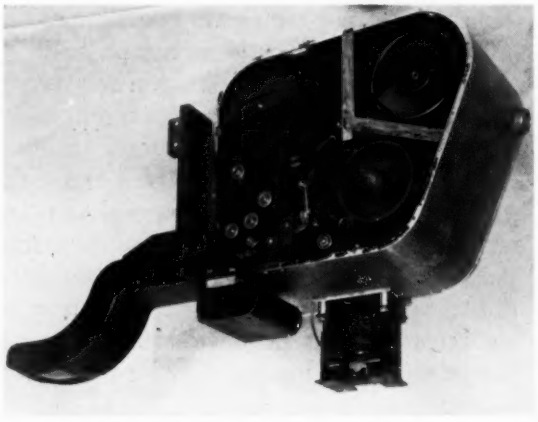

FIG. 4. Film-moving mechanism with side removed to demonstrate supply spool, take-up spool, metering roll, etc.

now mounted in the housing of the film-moving mechanism, as well as a cam-operated switch to activate a counter on the control stand and thus show the number of film "frames" that have been used and, by subtraction, the number remaining on the film supply spool. Bench testing with a variable speed motor has demonstrated that the film can be clamped to the button, released, advanced, and then reclamped at rates as high as 6 complete film cycles per second. During half of each cycle the film is stretched over the button and motionless so that at a transport rate of 6 frames per sec-

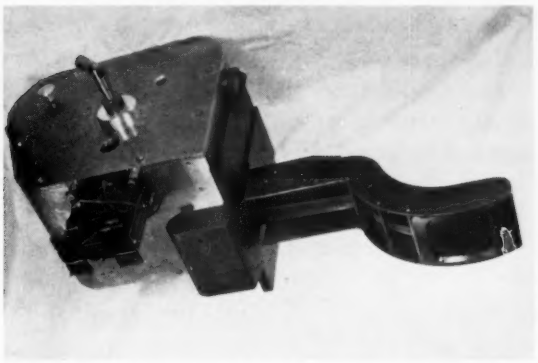

Fig. 5. The opposite side of the film-moving mechanism with the bottom of the film duct removed to show button and lever for activating button.

Fig. 6. Another view of the assembled camera to show power unit attached to drive shaft of film-moving mechanism.

ond the standstill time is 1/12 second and exposures may be as long as 1/20 second and still leave 1/60 second standstill before and 1/60 after each exposure. At 5 frames per second, exposures may be as long as 1/15 second; at 4 frames, 1/12 second; at 3 frames, 2/15 second; at 2 frames, 1/5 second; and at 1 frame as long as 7/15 second.

SPEED AND RESOLVING POWER

Theoretically the resolving power of this optical system is about 20 lines per millimeter and since the minification factor is about 7.5, this means something more than $2\frac{1}{2}$ lines per millimeter measured at the fluoroscopic screen and preliminary experiments suggest a resolving power considerably better than this. It has not yet been possible to make precise measurements of the speed of the system but it appears to be at least six times that of the f/1.5 Ektar, a speed that will be great enough to allow the making of acceptable microfilms of the skull, mediastinum and trunk at exposure times that are sufficiently short and with tissue doses of permissible magnitude.

CLINICAL APPLICATIONS

Figure 7 shows the camera temporarily installed for clinical testing. The patient climbs five steps to a platform about 40 inches above the floor of the room and then lies on a roentgen-ray table top that is about 28 inches above the level of the platform. Just enough space is left beneath the under surface of the table top and the convex upper surface of the aluminum spinning that carries the fluorescent screen for the insertion of a Liebel-Flarsheim crisscross grid. A Dynamax 25 roentgen tube is

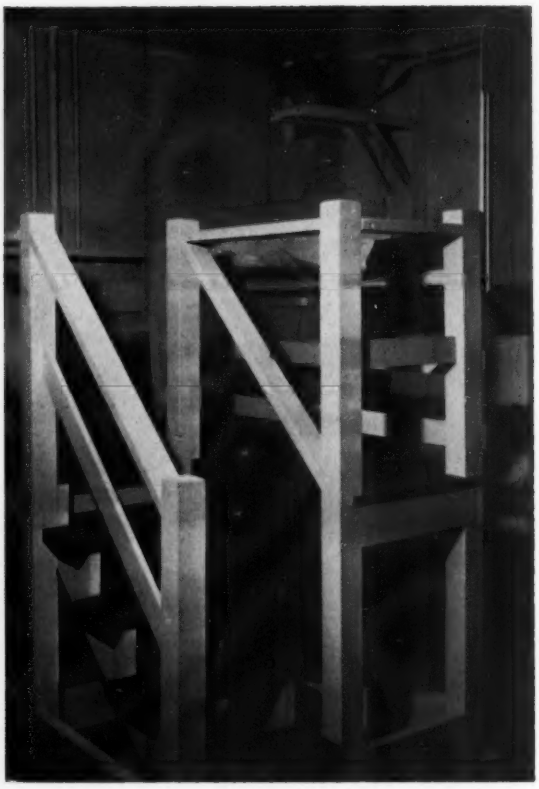

FIG. 7. Seventy millimeter camera temporarily installed for clinical testing. Under these circumstances the patient has to climb five steps to reach the roentgen-ray table but later the camera will be sunk in the floor of the room so that the table can be of standard height.

mounted on a bracket with its target 36 inches above the screen, but eventually we expect to replace this with a Super-Dynamax. Eventually a pit will be built into the floor of the room so that the base of the camera will lie below the floor with the hood projecting up beneath a roentgen-ray table of conventional height.

OTHER AMERICAN REFLECTOR CAMERAS

When this work was started, no reflector photofluorographs had been built in the United States and we were unaware of the instruments that were being developed in Denmark. Now five or more of the Danish cameras have been brought to this country and at least two other American cameras have been built. Dr. Morgan tells me he has had the opportunity to operate a reflector camera made by the Fairchild Company and, more recently, another having an optical system made by the Perkin Elmer Company, and finds both of them satisfactory.

If any one of these various optical systems proves distinctly faster than the others or has significantly better resolving power, then that one will be the system of choice, regardless of other considerations, but if speed and definition are about equal in all of them, then ease and cost of manufacture may become the factors on which preference must be based. This first 70 mm. reflector camera of ours is heavy and costly but additional instruments would cost much less and, with improved design, the weight could be reduced considerably. A great advantage of the Henyey-Greenstein optical system lies in the fact that its lenses are spherical rather than "figured" but, unlike the classical Schmidt, the Henyey-Greenstein system cannot conveniently be "folded." This requires installing the camera through the floor of the room in which it is to be used, a matter of little importance in new buildings but expensive and inconvenient in old ones.

CONCLUSIONS

1. After more than six years of work, a 70 mm. photofluorographic camera, employing a reflector optical system designed by Henyey and Greenstein, has been completed and is undergoing clinical testing.

2. Unlike the conventional Schmidt, this camera employs a doublet of spherically ground crown and flint glass rather than a "figured" plate glass corrector plate.

3. Preliminary testing indicates a speed more than six times that of the f/1.5 Ektar and a resolving power better than 20 lines per millimeter.

4. It is believed that the instrument will be useful for cardiac and cerebral angiography, as well as for the microfilming of the gastrointestinal tract, trunk and extremities.

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DISCUSSION

Dr. Russell H. Morgan, Baltimore, Maryland. I have three comments to make in regard to Dr. Hodges' paper.

First, I was delighted to hear him give a historical account of the development of the reflector camera which he has had under construction for some time. Many people gain the impression that research in projects such as this goes smoothly and rapidly. Such, however, is far from the truth. Developments of this sort require a lot of painstaking work, and I can assure you that pitfalls do occur much more frequently than do successes.

Dr. Hodges' paper illustrates, better than anything I could say, the problems which confront an investigator when he undertakes a project of this sort. I hope, however, it will not disturb nor discourage young men from undertaking similar problems, because I can also assure you that when one finally comes to success the pleasure and satisfaction that one gains from that success is very great indeed.

The second comment that I would like to make is relative to the camera itself. This camera appears somewhat bulky and, perhaps, for immediate application is not too practical; but I can say that as a result of Dr. Hodges' work in this field, the lens designers in this country have been stimulated to a degree of activity that would not have been achieved under other circumstances.

Even the people who are designing refractor lenses (that is, the conventional lenses with which you are familiar), recently have become interested in highspeed lenses, and the Eastman Kodak Company has just developed an excellent refractor lens for 35 mm. work. Undoubtedly, they will go on and will try their efforts at 70 mm. work, too.

I feel that all of this progress would have been delayed a good deal if it had not been for the stimulation and energy behind the work in this field which Dr. Hodges has carried on.

The final comment I have to make concerns the application of photofluorography in the clinical field. Dr. Hodges touched on it very briefly. It is my impression that in the not too distant future, when fast lenses become completely practicable, many radiologists in their offices and in hospitals will utilize photofluorographic equipment to provide a much wider range of radiological service to their patients than has heretofore been possible under the economics of present-day radiology.

The large films, I think, limit all of us in giving as much radiological service as we would like, and the photofluorographic method provides at least one mechanism for breaking through this seeming impasse to provide greater service to our patients without great economic stress to them.

AN AUTOMATIC REGULATOR FOR PROVIDING CONSTANT BRIGHTNESS OF THE FLUOROSCOPIC SCREEN*†

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ONE of the most difficult problems which has been encountered in the development of equipment for the intensification of fluoroscopic screens has been the design of apparatus which is both simple and convenient in clinical practice. Although enormous strides have been made in the development of equipment which provides increases in screen brightness of several thousand times or more, the various forms of apparatus which have been devised are, without exception, too complex in their operation for general clinical application. For example, in the Johns Hopkins screen intensifier, the operator is required to maintain surveillance over brightness and contrast controls, a black-level control and a control which governs the beam current of the image orthicon. This obviously interferes very materially with the clinical phases of a fluoroscopic examination. It has seemed to us for some time that if screen intensifiers are to become clinically worth while, they should be made essentially automatic so that the radiologist is not required to give any appreciable amount of time to their operation.

Almost all of the changes which the radiologist must make in the controls of a screen intensifier are caused by the changes in the illumination of the fluoroscopic screen which occur when one passes from the examination of one anatomical structure to another. It therefore follows that if one could arrange conditions so that the brightness of the fluoroscopic screen would remain constant as one passes from the chest to the abdomen, for example, the screen intensifier would operate smoothly without attention.

With this concept as a background, work was begun on the development of an automatic regulator for the provision of constant fluoroscopic screen brightness regardless of the anatomical structure being examined. The problem of designing such an instrument is essentially the same as that which confronted us when we developed the first photo-electric timer. In the case of the photo-electric timer, we were interested in the delivery of a constant quantity of radiation to the roentgenographic film, regardless of the anatomical structure under study. In the case of the instrument for maintaining constant screen brightness, we are interested in the delivery of a constant roentgen-ray intensity to the fluoroscopic screen, under the same conditions.

The basic elements of a photo-electric timer include a radiation detector (usually a multiplier phototube and an overlying fluorescent screen) which when placed under the roentgenographic film generates an electric current in response to the radiation exposure. The instrument also includes a thyratron-integrator circuit which sums up the current delivered by the phototube and which turns off the roentgen-ray machine automatically when the collected charge reaches a particular predetermined level.

The device which we have developed for automatically regulating the brightness of the fluoroscopic screen is shown in block diagram in Figure 1 and schematically in Figure 2. For convenience, we shall hence-

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† Presented at the Fifty-third Annual Meeting, American Roentgen Ray Society, Houston, Texas, Sept. 23–26, 1952.

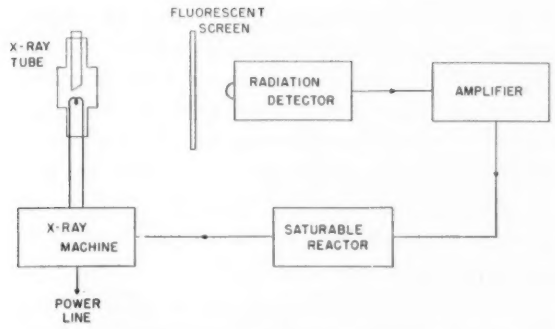

FIG. 1. Block diagram indicating the essential components of the fluororegulator.

forth refer to it as the fluororegulator. In these diagrams, it will be seen that the nucleus of the instrument, like that of the photo-electric timer, is a radiation detector which utilizes a multiplier phototube. The multiplier phototube, V_1, observes the fluoroscopic screen and in response to the light emitted by the screen, generates a small electric current. This current, however, is not fed into an integrating circuit as is the case in the photo-electric timer, but instead, is led directly to a simple single-stage amplifier, V_2, which includes the primary winding of a saturable reactor, Z, in its plate circuit. The secondary winding of the saturable reactor is connected in series with the primary winding of the filament transformer, T, which supplies the fluoroscopic roentgen tube. The current generated by the radiation detector therefore has control over the temperature of the filament of the roentgen tube and therefore has control over the roentgen tube current.

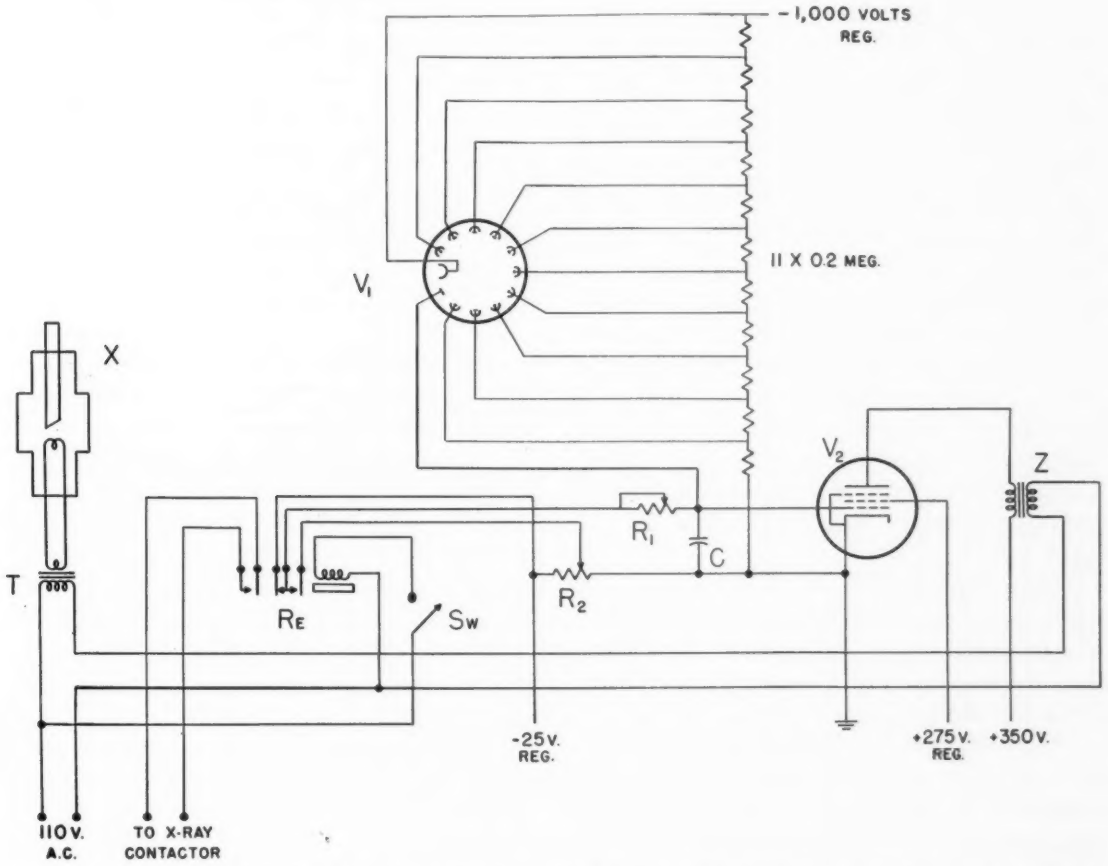

FIG. 2. Schematic diagram of the fluororegulator. V_1, R.C.A. 5819 multiplier phototube; V_2, R.C.A. 6BG6-G amplifier tube; R_1, 20 megohm variable resistor; R_2, 0.1 megohm variable resistor; C, 0.01 microfarad condenser; Z, saturable reactor; T, roentgen tube filament transformer; RE, relay; SW, fluoroscopic exposure switch.

Since the radiation delivered by a roentgen tube is directly proportional to the tube current, it is evident that the fluororegulator exercises control over the radiation output of the fluoroscopic roentgen tube.

To understand more clearly the operation of the fluororegulator, let us trace the series of events which occur first when a thin anatomical structure is under examination, and then when a thick anatomical structure is to be studied. When a thin structure is under the fluoroscope, the brightness of the fluoroscopic screen normally is quite high. If the fluororegulator is in the fluoroscopic circuit, the radiation detector of the device observes the fact that the screen brightness is at a high level and generates therefore a relatively large current. This current is amplified by the amplifier tube of the fluororegulator in such a way that the impedance of the saturable reactor in the roentgen tube filament circuit is caused to increase. Indeed, since the current generated by the radiation detector is relatively large, the increase in the impedance of the saturable reactor is large. This reduces the current delivered to the filament of the roentgen tube, thereby reduces the temperature of the roentgen tube filament, and hence lowers the radiation intensity delivered by the roentgen tube. As a result, when a thin structure is under the fluoroscope, the fluororegulator acts in such a way that the roentgen tube current and radiation intensity generated by the roentgen tube are reduced to relatively low levels.

When one moves the fluoroscope to a thick structure, the brightness of the fluoroscopic screen begins to diminish. The radiation detector of the fluororegulator recognizes this fact and the current which it generates also diminishes. Through the amplifier, this diminution in radiation detector current acts in such a way that the impedance of the saturable reactor also decreases. This causes the current in the roentgen tube to rise and the radiation output of the tube therefore increases. As a result, when the thick structure is under examination, the output of the roentgen tube automatically rises to higher levels than those which existed when a thin structure was under examination. Indeed, in actual practice, the changes in roentgen tube output almost entirely compensate for changes in anatomical part thickness to maintain the brightness of the fluoroscopic screen at a constant level.*

* The brightness of the fluoroscopic screen is proportional to the current flowing through the roentgen tube and to the roentgen-ray transmission of the anatomical structure under examination. This relationship may be expressed by the equation

$$I = kTi_x \tag{1}$$

where I is the brightness of the fluoroscopic screen, T is the roentgen-ray transmission of the anatomical structure, i_x is the roentgen tube current and k is a constant.

It is evident from this equation that if the brightness of the fluoroscopic screen is maintained constant, the current through the roentgen tube varies inversely with the transmission of the anatomical structure.

How well the fluororegulator may be expected to maintain the brightness of the fluoroscopic screen at a constant level can be determined from the following analysis. The current generated by the photomultiplier tube, V_1, in response to the light falling upon it from the fluoroscopic screen may be expressed by the equation

$$i_p = sI \tag{2}$$

where i_p is the phototube current and s is the sensitivity of the phototube.

Also, the relationship between phototube current and the current flowing through the primary winding of the saturable reactor, Z may be given by the expression

$$i_p = \frac{C - i_b}{g_m R_1} \tag{3}$$

where i_b is the plate current of the amplifier tube, V_2, g_m is the mutual conductance of this tube and C is a constant.

Now, the relationship between the current flowing through the primary winding of the saturable reactor and the current flowing through the roentgen tube is governed by the characteristics of the saturable reactor and the various components of the roentgen-ray generator and constitutes a rather complex function. However, the following simplified equation expresses this relationship sufficiently well for practical purposes:

$$i_x = a + bi_b \tag{4}$$

where a and b are constants.

When the equations (1) to (4) are combined and i_x is eliminated

$$I = [bC + a]\left[\frac{kT}{1 + sbg_m R_1 kT}\right]. \tag{5}$$

The value of the term, $sbg_m R_1 kT$, for the normal range of roentgen-ray transmission can be made much greater than unity by making R_1 large (*e.g.*, 20 megohms). Under these conditions equation (5) becomes

$$I = \frac{[bC + a]}{sbg_m R_1}. \tag{6}$$

Since the right hand term of equation (6) includes only constant parameters, the brightness of the fluoroscopic screen remains constant and is unaffected by changes in roentgen-ray transmission.

In Figure 3, the performance characteristics of the fluororegulator are shown graphically. Here the brightness of the fluoroscopic screen is plotted as a function of the roentgen-ray transmission of the anatomical structure under examination. It will be observed that the brightness of the fluoroscopic screen may be maintained at a relatively constant level over a wide range of fluoroscopic conditions. For example, if the structure under examination is the chest (transmission = 10 per cent), the brightness of the fluoroscopic screen is almost identical to that which prevails when no structure is placed in front of the fluoroscopic screen (transmission = 100 per cent). Furthermore, when the abdomen (transmission = 1 per cent) is examined, the brightness of the fluoroscopic screen is only diminished by a few percentage points. When one passes finally to an examination of the lateral lumbar spine (transmission = 0.1 per cent) some loss of control occurs. Even here, however, the drop in screen brightness necessarily need not be great. Indeed, as will be shown in a moment, the loss in screen brightness with very thick structures is limited only by the level of fluoroscopic milliamperage to which one is willing to go.

If the brightness of a fluoroscopic screen is maintained at a constant level regardless of the anatomical structure being studied, it follows that the milliamperage of the roentgen-ray tube must vary through a wide range when one passes from the examination of thin structures to that of thick structures. This fact is graphically shown in Figure 4 where the roentgen-ray tube current is plotted as a function of roentgen-ray transmission. It will be observed that the roentgen tube current is almost inversely proportional to roentgen-ray transmission over most of the latter's range. The shape of the curve is characteristic of the fluororegulator. The curve, however, may be raised or lowered on the roentgen tube axis by raising or lowering the current through the primary winding of the saturable reactor of the fluororegulator by

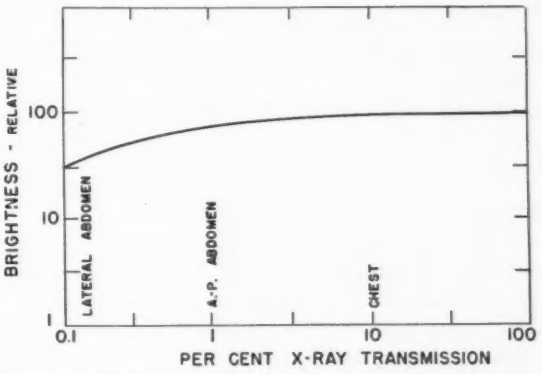

FIG. 3. Relationship between fluoroscopic brightness and the transmission of the anatomical structure under examination when the fluoroscope is controlled by the fluororegulator. Observe that the instrument maintains the brightness of the screen relatively constant through the wide range of fluoroscopic conditions normally encountered in fluoroscopy.

means of the amplifier control, R_2, shown in Figure 2. The curve may be displaced to the right or to the left by decreasing or increasing respectively the amplification of the amplifier of the fluororegulator by the control, R_1, shown in Figure 2. Hence, it

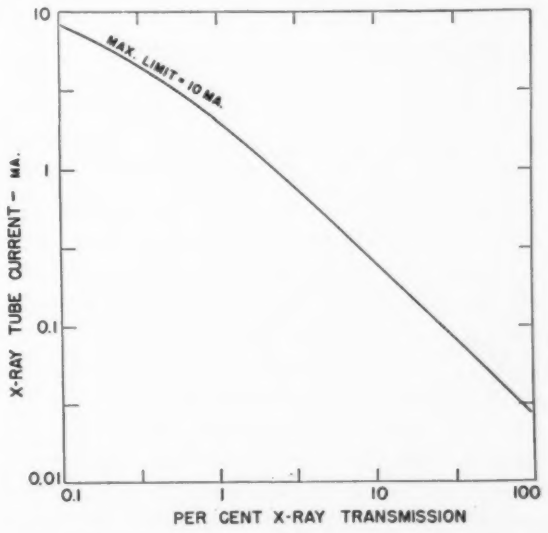

FIG. 4. Relationship between roentgen tube current and the roentgen-ray transmission of the anatomical structure under examination, when the fluoroscope is operated under the control of the fluororegulator. Note that the roentgen tube current is almost inversely proportional to the roentgen-ray transmission of the anatomical structure over major portions of its range.

is possible to set the fluororegulator to provide almost any range of control which one desires.

It will be observed that if one adjusts the fluororegulator so that the roentgen tube current is 2 milliamperes for normal abdominal fluoroscopy and reaches a top limit of 10 milliamperes when no radiation reaches the fluoroscopic screen, the fluoroscopic tube current for chest fluoroscopy falls to a level of 0.25 milliampere. When no structure is present in the roentgen-ray beam, the milliamperage falls to 0.025 milliampere.

From the standpoint of its ability to maintain the brightness of the fluoroscopic screen at a constant level, the fluororegulator appears to function very satisfactorily. When used in conjunction with a screen intensifier such as the Johns Hopkins type, it will effectively eliminate the need for the radiologist to devote any significant amount of time to the adjustment of the instrument. His time, therefore, will be free for the clinical phases of his examinations. We therefore anticipate that the fluororegulator will form a very important part of our screen intensification system.

Although the fluororegulator was designed primarily for use in conjunction with screen intensification systems, it may have application in standard fluoroscopy. Here it would constitute an automatic safeguard which would tend to reduce roentgen tube currents when the shutters of the fluoroscope are opened widely. Furthermore, it would provide on an automatic basis higher levels of screen brightness and therefore better visibility when very thick structures are examined. This latter characteristic may perhaps seem somewhat dangerous. However, if the fluororegulator is adjusted so that the roentgen tube current under any circumstance cannot exceed a predetermined safe level, this danger will not be present.

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DISCUSSION

DR. PAUL C. HODGES, Chicago, Illinois. This compensating, stabilizing device that maintains screen brilliance at a constant level is indeed clever and should be useful. I suspect that this audience includes many radio and television enthusiasts who know much more about circuits of this sort than I do.

I think Dr. Morgan is too modest in his statements about the possible application of his circuit outside the field of image amplification. Probably it will find a place in ordinary fluoroscopy as well where it will keep the dose down during the examining of thin parts, thus making it safer to let the dose go up during those few seconds devoted to the examining of heavier parts.

What I most want to say has to do with the whole field of image amplification rather than this specific phase of it. I want to urge all of you not to be discouraged at the slowness with which the clinical stage is reached. Dr. Morgan has just shown us the first clinical motion picture that he has been able to make with the aid of his image amplifier, but much work remains to be done before such motion pictures can be employed in routine clinical work. As we review the history of the development of television, we are reminded that it, too, developed slowly. In this matter of image amplification, development has been and will continue to be slow, but we have nothing to worry about as long as the investigation continues and I, for one, am absolutely certain of ultimate success. Physical laws are inescapable, as Dr. Morgan has just told us, but clever men are prone to find ways around inescapable difficulties, and even this obstacle of graininess which at the moment Dr. Morgan believes is insuperable probably will be overcome by some ingenious flanking attack.

Vol. 71, No. 1

A SIMPLIFIED METHOD OF CORRECTING ROENTGENOGRAPHIC MEASUREMENTS OF THE MATERNAL PELVIS AND THE FETAL SKULL*

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THE different methods of correcting for the divergence of the roentgen-ray beam when measuring the diameters of the maternal pelvis and the size of the fetal skull may be placed roughly in four groups: (1) the geometric, in which calculations are made according to the target-film and the object-film distances, (2) the metal centimeter marker, placed at the same distance from the film as the diameter or object to be measured and photographed on the film, (3) the precision stereoscope, and (3) the parallax method in which the apparent shift of the film image, produced by shifting the roentgen tube, is used to calculate the correction factor. Any of these methods carried out accurately and carefully will give satisfactory clinical results. Each has certain advantages and disadvantages which cannot be discussed here.

The purpose of this communication is to present a simple method of calculating the correction factor for a measurement on a roentgenogram where the object-film distance is known and the target-film distance is 100 cm. (39–40 inches).

In 1936 Ball described a geometric method for measuring the pelvic diameters and the volume of the fetal skull using a nomogram to make the corrections for the exaggeration of the shadows caused by the divergent roentgen-ray beam. Ball and Golden (1943) described certain advantages when the patient was roentgenographed in the erect position. Holmquest (1938) published a revised monogram which is available in sheet form for reporting individual cases.

The technique described by Ball and Golden continues to be used at the Presbyterian Hospital with two modifications: (1) With the patient erect, the shadow of the pubic bone sometimes obscures that of the ischial spines. To throw the shadow of the pubic bone down farther, the tube is moved up 15 cm. (6 in.) from the level used for the lateral view. As can be shown mathematically, moving the tube up or down any desired amount or angling it any desired degree does not affect the measurement, provided that the perpendicular target-film distance remains the same. As suggested by Ball and Golden, erect stereoscopic views can be taken in the anteroposterior projection to study the shape of the pelvis ("pelviography" according to Caldwell and Molloy). (2) The development of the 16 to 1 grid has improved the "clean-up" qualities of the Potter-Bucky diaphragm. The 16 to 1 grid requires a target-film distance of 40 inches which is practically 100 cm. This is now the routine target-film distance at the Presbyterian Hospital for pelvimetry films for the Ball method.

CORRECTION FACTOR

A calculation, so simple that it can be done mentally, will give the correction factor for any structure lying approximately parallel to the film, provided the target-film distance is 100 cm. (39–40 in.). It is particularly well suited for the pelvicephalometric method originated by Ball, but can be used with any system in which the object-film distance can be determined. This calculation is applicable to both anteroposterior and lateral projections.

According to the rule of similar triangles it follows from Figure 1 that

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$$b:x=a:i \qquad \text{Equation I}$$

when b is the target-object distance
a is the target-film distance
x is the true size of the structure to be measured, and
i is the size of the film image of the same structure.
It is also apparent from this illustration and inherent in the definition of a and b that

$$b=a-d \qquad \text{Equation II}$$

when d is the object-film distance.
Developing equation I, one obtains thus:

$$b:x=a:i$$

$$x=\frac{i\cdot b}{a}=i\cdot\frac{b}{a}$$

Substituting equation II for b, one obtains thus:

$$x=i\cdot\frac{a-d}{a} \qquad \text{Formula I}$$

If one selects a target-film distance (a) of 100 cm. which is approximately 39–40 inches:

$$x=i\cdot\frac{100-d}{100}$$

All the observer has to do in this case, therefore, is to subtract the object-film distance in centimeters from 100. The result represents directly that number of per cent of the measured diameter which constitutes the true diameter, *e.g.*, if the object-film distance is 10 cm., 100−10=90 indicating that the true diameter is 90 per cent of the measured diameter. If the object-film distance is 14 cm. the true diameter is 100−14=86 per cent of its roentgen image, etc.; in short, the correction factor is 0.9 in the former and 0.86 in the latter case.

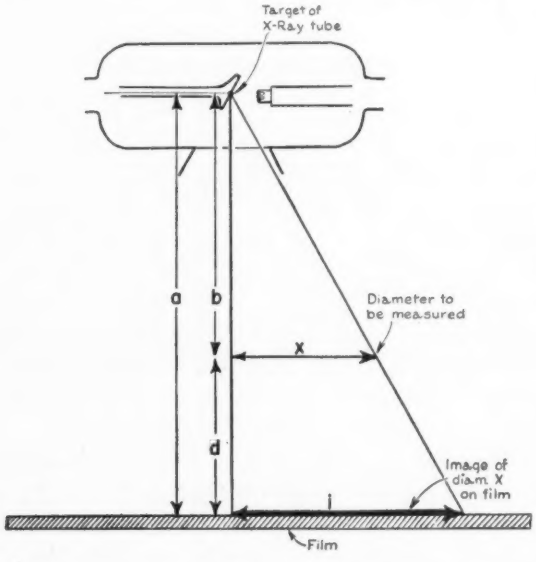

FIG. 1

If this calculation is applied to films taken at a target-film distance of 36 inches (91.5 cm.) it will produce results which are slightly too high. The error is then approximately 1 per cent at an object-film distance of 10 cm., 2 per cent at an object-film distance of 20 cm. and 4 per cent at an object-film distance of 30 cm. However, 6:1 or 8:1 grids, customarily focused for a 36 inch target-film distance can be used at a 40 inch distance without adversely affecting the roentgen image. This is in striking contrast to the 16:1 grids as they are now constructed which cannot be used at a 36 inch distance without loss of image quality. They can be adapted to distances greater than 40 inches, however, with some measure of success.

CORRECTION BY SLIDE RULE

A simple slide rule has been constructed which determines the correction factor and corrects the measured diameter in a single operation. In its most primitive form it contains an object-distance scale (from 0 cm. to 40 cm.) and a pair of identical standard logarithmic scales (from 3 cm. to 50 cm.). One of these is made to represent the values for the measurement obtained from the film, whereas the other designates the corrected values. An arrow on the slide is set at the object-film distance of the structure to be measured which is shown on the first, or uppermost, of the three scales described above. The uncorrected dimension of the structure obtained from the film is shown on the third, or lowermost, scale and the corrected value is shown immediately above it on the second scale located on the slide. The corrected value,

therefore, can be read immediately on the slide rule. The spread of the object-film distance scale is identical with that of the other two scales.

As has been shown above, the mathematical correction according to formula 1 is particularly simple when the target-film distance is 100 cm. Taking advantage of this condition one can construct such a slide rule for this target-film distance (39 to 40 in.) with particular ease. It is possible then to transform a standard logarithmic scale into an object-film distance scale merely by relabeling its unit numbers as follows:

10 becomes 0 cm.
9 becomes 10 cm.
8 becomes 20 cm.
7 becomes 30 cm., etc.

All divisions and subdivisions of this scale remain unchanged.

Slide rules for target-film distances other than 100 cm. must have different object-film distance scales which cannot be obtained by simple relabeling. For example, for a target-film distance of 36 inches:

91.5 on the logarithmic scale must become 0 cm.
81.5 on the logarithmic scale must become 10 cm.
71.5 on the logarithmic scale must become 20 cm., etc.

None of the existing divisions of a standard logarithmic scale can be used, therefore, for the making of such a scale because all centimeter values fall between its divisions. A complete redrawing of a logarithmic scale for the object-film distance scale is, therefore, necessary.* Once this is done, however, such a slide rule is as simple to use as that for a target-film distance of 100 cm.

It is possible to preserve this single operation principle and yet make the slide rule applicable to a variety of target-film distances† by incorporating a separate object-film distance scale for each target-film distance to be used, all of which are made to act upon the excursion of the same slide. The user of such a slide rule has to select the correct object-film distance scale on the face of the slide rule from a choice of *e.g.* three such scales (30 in., 36 in, and 40 in.), but as before only a single operation is necessary and consists merely of setting the slide by moving an arrow to the correct object-film distance, whereupon the final corrected value will appear on a scale opposite the measured figure.

The usefulness of this principle of single operation can be developed further by adding volume scales and a fetal age scale to the slide rule. Since each pelvic diameter is assigned only one volume capacity by the Ball method and since each mean circumference of the fetal head is assumed to correspond to only one volume, the relationship between volume and corrected film measurements is fixed. By printing the volume scales in the proper location relative to the corrected dimension scale on the same slide, one obtains a device which will indicate volume capacity and fetal head volume instantly and without any additional operation any time a corrected diameter or circumference measurement is obtained.

In the same manner a fetal age scale can be printed on the same slide above that part of the corrected dimension scale which contains the corrected values of fetal skull circumferences. Utilizing Hodges' modification of the formula of Scammon and Calkins, it is apparent that the relationship between mean skull circumference and average fetal age is sufficiently fixed to permit this. Again, no additional operation is necessary.

Finally, the operation of this slide rule can further be simplified by adapting it

* An exception to this is the target-film distance of 2 meters. For this distance 20 becomes 0 cm., 19 becomes 10 cm., 18 becomes 20 cm., 17 becomes 30 cm., etc.

† Roentgenometric slide rules have undoubtedly been constructed on this or a similar principle before. When they are adapted to more than one target-film distance at least one additional setting operation is required. This makes their use more exacting and introduces the possibility of error because during the second operation the first setting may be dislodged. Other slide rules work on the single operation principle but require the calculation of a correction factor from a table or a formula before the slide can be set.

also to the centimeter metal marker system. By attaching one pointer to the body of the slide rule and another to the moving slide, one obtains a caliper. The spread of the logarithmic scale can be so chosen (270 mm. per cycle) that the image of a 10 cm. long metal ruler is enlarged on the film (over its actual length of 10 cm.) by the same amount as is necessary to move the slide of the slide rule in order to obtain the correction for this enlargement. Regardless of target-film distance or object-film distance the slide will then always be set correctly when the two caliper pointers encompass 10 divisions of the film image of the centimeter marker. The operation of the slide rule is thus reduced to placing the caliper on the film over the image of the metal marker and reading the result on the corrected dimension scale on the slide rule opposite to the measured value. A slide rule incorporating all the features described above is illustrated in Figure 2.

A slight inaccuracy is incurred by this caliper method because it is mathematically incorrect to correlate a linear function (enlargement of the metal ruler) to a logarithmic function (shift of the slide). However, if the excursion of the slide is limited to a maximum caliper span of 14.5 cm., the

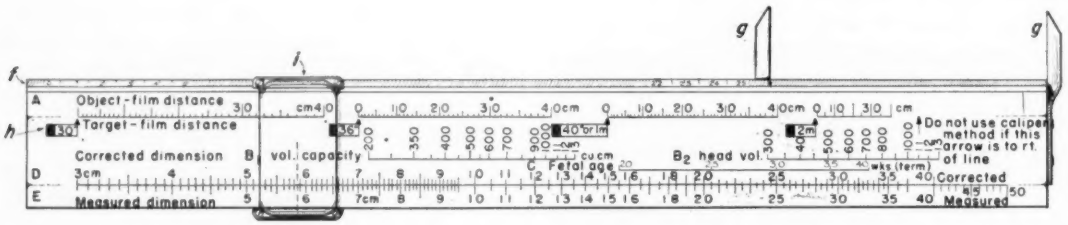

FIG. 2. Front view of slide rule, reduced from 14⅝ inches (37 cm.). Certain details are omitted for better legibility in reproduction. Each arrow in row "*h*" is labeled with a different target-film distance and opposes one of the four object-film distance scales "*A*." A concealed built-in stop limits the excursion of the slide so that each arrow can oppose only the correct object-film distance scale for which it is labeled. The bevelled edge "*f*" bears a general purpose centimeter ruler.

The indicator "*i*" possesses a shortened hair line which avoids scale "*A*" and the arrows in row "*h*." This indicator is a visual aid but not essential for the operation of the slide rule. The caliper pointers "*g*"—designed for an alternate method of operation—are to be placed upon the film image of a metal marker. Their use as well as the purpose of the scales and the indicator are explained on the back of the slide rule, as follows:

1. Select the arrow labeled with the target-film distance employed and move this arrow to the previously determined* object-film distance on Scale A.
2. Move the hairline to that figure appearing on Scale E which represents the pelvic diameter or the circumference of the fetal skull as measured on the film; the corrected value is now shown by the hairline on Scale D.
3. If the hairline also intersects Scale B-1, the volume capacity of this corrected diameter is shown on this scale in terms of a sphere.
4. Having obtained the corrected circumference of the fetal skull in both AP and lateral projections, determine the average of the two figures which is the MEAN CIRCUMFERENCE. Set the hairline on the figure on Scale D which represents this MEAN CIRCUMFERENCE and read the volume of the fetal head on Scale B-2 which is corrected to include the scalp.
5. The hairline in step 4 also intersects Scale C and indicates the approximate fetal age in weeks correlated with the mean circumference of the fetal skull, as adapted from Hodges' modification of the Scammon and Calkins formula.

1a. (Caliper method for use with metal ruler). Move slide until image of 10 cm. long metal ruler or of 10 divisions of a graduated cm. metal marker fits between caliper pointers and proceed with step 2, 3, 4 and 5 as above. (Valid for any target-film distance).

The back of the slide rule also bears a table of normal average pelvic diameters.†

* See Instruction Booklet.

† A slide rule of this type will be made available by the Picker X-ray Corporation.

maximum error is kept within ±1.4 per cent, the average error being less. This caliper method of slide rule operation cannot be applied then to the correction of dimensions, the object-film distance of which is longer than 31 cm. at a target-film distance of 40 in., 28.5 cm., at a target-film distance of 36 in., or 24 cm. at a target-film distance of 30 in. A warning sign on the slide rule indicates when this maximal permissible excursion has been exceeded. In this case, the original object-film distance method of slide rule operation can be employed as described above and in the legend of Figure 2. Fortunately, there is no limit to the permissible excursion of the slide with this method; in fact, a range from 0 to 40 cm. could be provided for the object-film distance settings on the slide rule.

The above described maximum error of 1.4 per cent occurring with the metal marker-caliper method is quite comparable to the error incurred by the object-film distance method through no fault of the slide rule but due to the impossibility of measuring the bitrochanteric diameter on the patient's skin with absolute accuracy. A deviation of the so determined object-film distance by 1 cm. will produce an error of 1–2 per cent, depending on the target-film distance used. Both methods are thus equivalent, as far as accuracy is concerned, and it remains merely a matter of convenience which method is to be preferred in a particular instance. One can also use the caliper method for the lateral view and the object-film distance method for the anteroposterior view of the same patient.

SUMMARY

A simple mental calculation is described which yields, from the object-film distance, a correction factor for any linear dimension (curved or straight) measured on a roentgenogram, provided that the structure producing the roentgen-ray image lay parallel to the film and provided a target-film distance of 39–40 inches or 100 centimeters was used. The correction factor is obtained by subtracting the object-film distance in centimeters from the target-film distance of 100 cm. The particular advantage of making a simplified single operation slide rule for this target-film distance is discussed. A more elaborate single operation slide rule is described also which can be used for a variety of target-film distances and yields volume capacity of pelvic diameters, volume of fetal head and the corresponding fetal age without any additional effort or manipulation. It can be used with the centimeter metal marker method as well as with the object-film distance method. With the former it is independent of target-film distance and can be used in caliper fashion. Its two pointers, if placed on 10 divisions of the centimeter metal marker image, set the slide automatically.

Cephalopelvimetry is merely one of the adjuvants used in the process of arriving at an obstetrical opinion in regard to the possibility of a spontaneous delivery. Such an opinion is based on the consideration of many other factors such as uterine force, amount of molding, availability of compensatory space, fetal abnormalities, fetal position, systemic disease of the patient, etc. The extent to which this opinion will be influenced by a set of anatomical roentgen measurements will vary with the individual case and depends on the clinical judgment of the obstetrician and radiologist. Experience has shown that often cephalopelvimetry is of particular value in reassuring the referring physician that the dimensions of the bony pelvis are sufficient to permit a spontaneous delivery in a questionable case.

The clinical application and interpretation of cephalopelvimetry falls entirely outside the scope of this paper. The material here presented deals exclusively with the technique of this method and its simplification and is based purely on mathematical considerations.

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VOL. 71, NO. 1

A GENERAL FORMULA FOR PELVICEPHALOMETRY*

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METHODS for measuring the visualized anatomical parts have been of great interest to radiologists, especially in pelvicephalometry.

In pelvimetry, both on the anteroposterior and lateral views, methods of measurement have been satisfactory, since here we are dealing with horizontal diameters in fixed anatomical planes which can be localized. Each of these diameters lies in one plane only. Knowing the level or plane of these diameters, we can determine the correction factor for the magnification of the diameters on the film by placing a centimeter scale at these levels prior to the exposure. Obviously, the diameters to be computed and the centimeter scale will each be magnified on the film in the same proportion.

In cephalometry, the diameters of the fetal head are rarely horizontal, nor are they in a fixed plane. Therefore, in order to solve this problem we must develop a method whereby we can determine the correction factor for magnification regardless of the plane in which the fetal head lies.

The formula then must be a general formula which takes into consideration all three dimensions of space. For practical purposes, the formula and the roentgenographic technique must be simple.

The method to be presented offers no new principles, but its simplicity and general application to all problems of measurement warrant its presentation.

ROENTGENOGRAPHIC TECHNIQUE

Solution of the problem requires two exposures and the use of a marker to denote the X and Z axes on the film as suggested by Manganiello.[3]

The marker is centered and fastened on the cassette in order to prevent a shift of the marker image from the true axial line on the second exposure.

The simplest and most practical marker is a thin rectangular piece of metal, such as an ampule file, with a notch in the center of one side. Cassettes are marked with intersecting central lines which correspond to the X and Z axes on the films. The notched side of the marker is placed along one axis thereby avoiding any possible error as to which side of the marker is the axial line. The notch is centered on the other axis, and the marker is attached to the cassette with adhesive tape.

The first exposure is made with the roentgen tube in the central position. The central ray of the tube is directed to the center of the marker and film. The second exposure is made with the tube at the same height but after the tube has been shifted horizontally 4 to 6 cm. The tube is shifted on its arm across the Potter-Bucky table toward the patient's right side. As viewed on the film, the tube shift will be parallel to the X axis.

This standard procedure serves to identify the direction of the tube shift which must be known in choosing the proper image for measurements.

The two exposures may be made on a single film or on two separate films. For cephalometry with breech presentation, both exposures are always made on a single film. For cephalometry in head presentation or pelvimetry, separate films are used for each exposure in order to assure clear detail which otherwise might be obscured by overlapping pelvic shadows.

Whenever the exposures are made on separate films it is advisable to use two markers: one for each cassette. These markers should be centered and attached on the cassettes before the exposures are made to avoid delay between exposures.

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The cassette-locking device on the tray assures a central position of the cassette in the long axis of the table. However, there is no similar device for centering the cassette along the other axis. Therefore, when using two separate films, it is possible that the second cassette may be placed slightly lower or higher in the tray than the first cassette. In such cases, the axial lines of the X axes on the two films would not coincide. In order to prevent such an error it is advisable that each cassette be placed in the tray with one edge of the cassette against the lower or upper edge of the tray.

The fetal head is ovoid in shape. If the roentgen tube is too close to the fetal head it is conceivable that the most divergent rays striking the head will project a diameter shorter than the desired diameter. McElin *et al.*[4] quote Millington's criticism of the vertical tube-shift method for this reason. This error is not likely to occur if the target-film distance is 100 cm.

Breech presentations are always taken in the anteroposterior position since the fetal head lies in a lateral or quasi-lateral position. Vertex presentations are taken in both posterior oblique positions, since the fetal head frequently lies in an oblique position. If the head is engaged, it should maintain the same position relative to the maternal pelvis. The two oblique positions for exposures, being at right angle to each other, should produce quasi-frontal and lateral views of the fetal head (Fig. 7 and 8).

In computing the biparietal diameter of a fetal head, the supraorbital line is used as a guide. Obviously, the biparietal diameter must be on a line parallel to the supraorbital line (Fig. 7).

A restraining band is used across the patient's abdomen during the exposures to minimize possible fetal motion. In breech presentation, the band tends to maintain the fetal head in a horizontal position.

The average exposure requires about one and one-half seconds. Both exposures can be made in about five seconds, which is sufficiently short for the patient to hold her breath throughout the entire procedure.

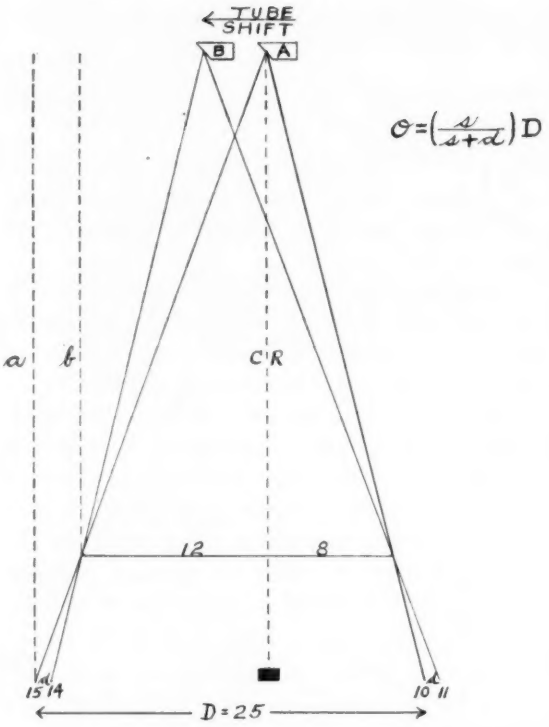

FIG. 1. Diagram for horizontal diameters. Note that the diameters of the two images are equal and that the two displacements are equidistant.

Horizontal Diameters. The geometric diagram in Figure 1 illustrates what happens by using this roentgenographic procedure when dealing with horizontal diameters. The two images of a horizontal diameter will be equal in length and parallel to each other. The two displacements or the distances between the corresponding ends of the images will be equal.

From this diagram the basic formula derived is the correction factor:

$$\frac{s}{s+d} = \frac{\text{tube shift}}{\text{tube shift} + \text{displacement of second image}}$$

In the diagram the letters have the following denotations:

A—First position of the roentgen tube
B—Second position of the roentgen tube
s—Tube shift
O—Actual object or diameter to be computed
D—Diameter of images
d—Displacements of second image
a—Target film distance
b—Target-object distance

In this diagram we note:

(1) $$\frac{b}{a}=\frac{s}{s+d}$$

and

(2) $$\frac{b}{a}=\frac{O}{D}$$

Therefore

(3) $$O=\left(\frac{s}{s+d}\right)D$$

Where:

$s=4$ cm.

$D=(10+15)$ and $(11+14)$ or 25 cm.

$d=(11-10)$ and $(15-14)$ or 1 cm.

Substituting the values for solution:

$$O=\left(\frac{4}{4+1}\right)25=20 \text{ cm. Actual size}$$

In roentgen pelvimetry we are dealing with horizontal diameters. In Figure 2, *A* and *B*, the pelvic inlet was computed from the lateral view of the pelvis. The tube shift was 5 cm., parallel to the *X* axis. The isometric method was used for comparison whereby 5 cm. of the actual serrated scale measured 6.4 cm. on its images.

Measurements obtained were as follows:

Film	Images of Pelvic Inlet (*D*)	Distances from Ends of Images to *Y* Axis	
3(a)	13.3 cm.	0.2 cm.	8.1 cm.
3(b)	13.3 cm.	1.6 cm.	9.5 cm.
Displacements (*d*)		1.4 cm.	1.4 cm.

Correction factor by isometric method:

$$\frac{5}{6.4}=0.78$$

Correction factor by author's method:

$$\frac{s}{s+d}=\frac{5}{5+1.4}=0.78$$

Solution by either method: $0.78\times13.3=10.37$ cm.
Other diameters of the pelvis can be computed similarly.

Figure 3 shows a breech presentation with the exposures made on a single film. The tube shift was 5 cm. Since the occipitofrontal diameters of both images are equal and both displacements are equidistant, this fetal head lies in a true horizontal position. Therefore, solution only requires direct application of the correction factor to the fetal skull diameters.

Measurements obtained were as follows:

Occipitofrontal diameters	15.6 cm.
Suboccipitobregmatic diameters	13.0 cm.
Displacements	1.5 cm.

$$\text{Correction factor}=\frac{s}{s+d}=\frac{5}{5+1.5}=0.77$$

Occipitofrontal diameter $=0.77\times15.6=12.0$ cm.
Suboccipitobregmatic diameter $=0.77\times13.0=10.0$ cm.
The postnatal measurements were 12.0 and 10.0 cm. respectively.

Nonhorizontal Diameters. Whereas, in pelvimetry we are dealing with horizontal diameters, in cephalometry horizontal diameters are the exception. Therefore, for a formula to be of any practical value in cephalometry, it must be applicable to all problems, regardless of the position of the fetal head.

A general formula derived for computing the distance between any two points in space must consider three dimensions. The computation of such a distance involves two right angle triangles; a horizontal triangle and a vertical triangle. These two triangles have two points (one side) in common, in that the hypotenuse of the horizontal triangle also forms the base of the vertical triangle (Fig. 4). Therefore in Figure 4

(1) $$X^2+Z^2=W^2$$

(2) $$W^2+Y^2=O^2$$

Substituting for *W* in (2)

(3) $$O^2=X^2+Y^2+Z^2$$

and

(4) $$O=\sqrt{X^2+Y^2+Z^2}$$

Where:
O is the actual size of the object or diameter to be computed, and *X*, *Y and Z* represent the sides of the triangles corresponding to their respective axes.

However, the above formula is the final step in the solution of any problem. The correction factors for distortion of the images on the films must be derived by which the actual values of *X*, *Y* and *Z* are computed.

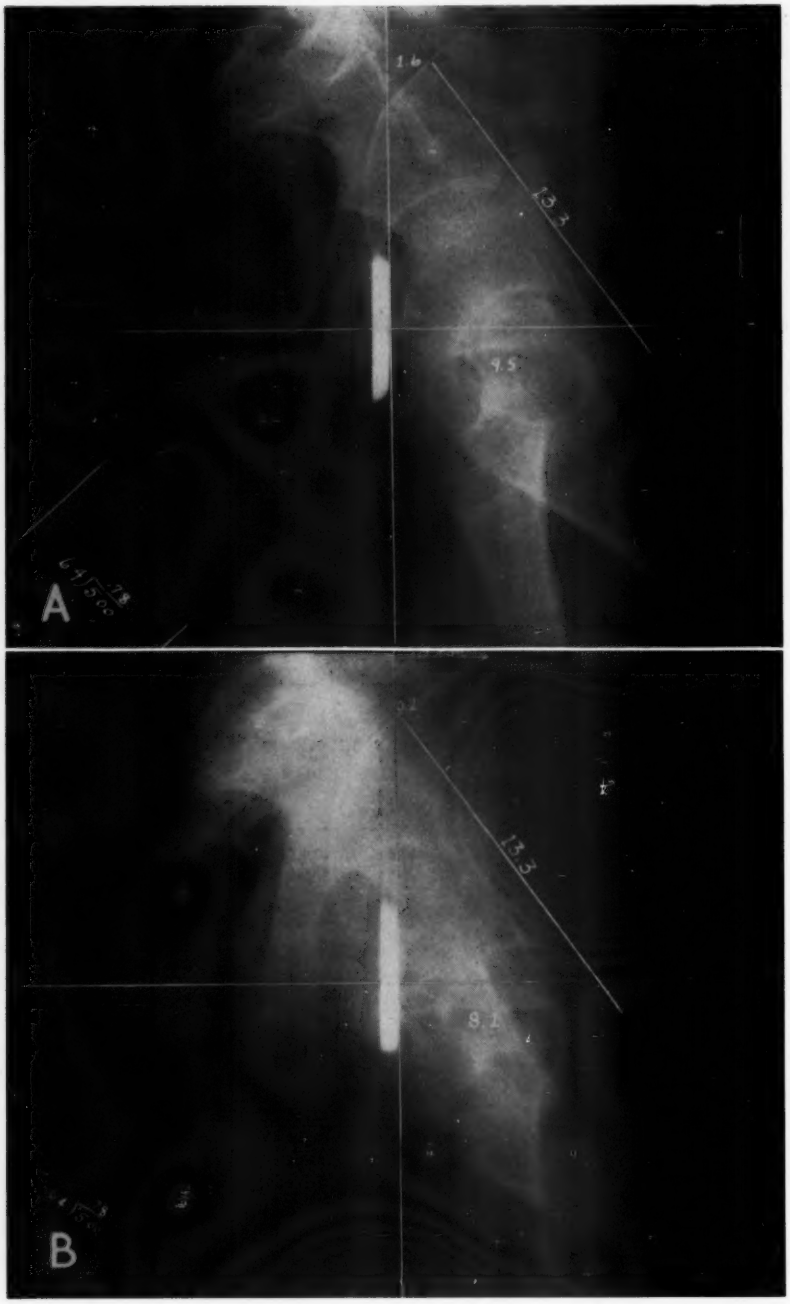

FIG. 2. (*A*) and (*B*). Horizontal diameters in pelvimetry computed by the isometric and author's methods. Exposures made on separate films.

Measurement Technique. Since the problem involves two right angle triangles with a common side, the two triangles with sides 3, 4, 5, and 5, 12, and 13 respectively are used as a convenient graphic illustration of the method of measurement and for derivation of the formula (Fig. 5). In this diagram the object or diameter to be computed is denoted by the letter "*O.*" The target-film distance is 40 cm., and the tube shift is 4 cm. The film portion of the diagram shows the relative positions of the two images of the object in relation to the *X* and *Z* axes denoted by the marker image.

Six measurements are made: the two coordinates of the *X* axis, the two coordinates of the *Z* axis, and the displacements of the second exposure image at each end of the object or diameter to be computed. The coordinates of

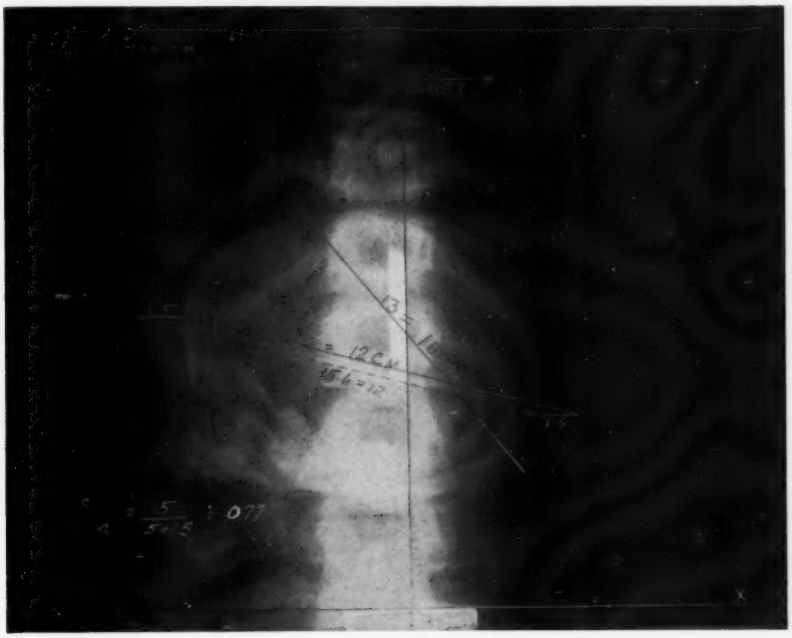

FIG. 3. Horizontal diameters in cephalometry with breech presentation. Both exposures made on the same film.

the axes (D), used in the derived formula, are always measured from the ends of the diameter of the *first exposure image*. This image lies further to the side toward which the roentgen tube was shifted. When the exposures are made on separate films, the images can be compared by superimposing the one film upon the other, or by the distances of the ends of the images from the Y axis. The displacements are the distance between the corresponding ends of the same diameter on the two images. The corresponding ends lie in a straight line parallel to the direction of the tube shift. *Since the tube shift is parallel to the X axis, the displacements are always measured parallel to this axis.* When the exposures are made on separate films, the coordinates of the X axis are measured on both films. The differences between the corresponding coordinates are the displacements.

Derivation of the Formula. By using this method of roentgenographic technique and measurement the general formula derived is:

$$X,\ Y,\ \text{or}\ Z = \left(\frac{s}{s+d}\right) D$$

The letters used in deriving the general formula have the following denotations:

O	Object or diameter to be computed.
P_1 and P_2	Ends of the object.
X, Y and Z	The sides of the two imaginary triangles formed with the object. The sides are designated by the corresponding axes.
X_1 and X_2	The distances, parallel to the X axis, from each end of the object to the Z axis.
Z_1 and Z_2	The distances, parallel to the Z axis, from each end of the object to the X axis.
D_1 and D_2	The distances from the ends of the first exposure image of the object to either the X or Z axis or to the target. Therefore, D_1 and D_2 each represent any one of three coordinates depending upon which axial component is being computed. The target-film distance is used for both D_1 and D_2 in computing the components of Y.
d_1 and d_2	The displacements of the ends of the second image from the corresponding ends of the first image.
s	Shift; amount of shift of roentgen tube.
a	The target-object distance.
b	The object-film distance.

Solving for the X and Z components in Figure 5:

(1) In the first exposure,

$$\frac{a}{a+b} = \frac{X_1}{D_1}$$

(2) In the second exposure,

$$\frac{a}{a+b} = \frac{X_1+s}{D_1+s+d_1}$$

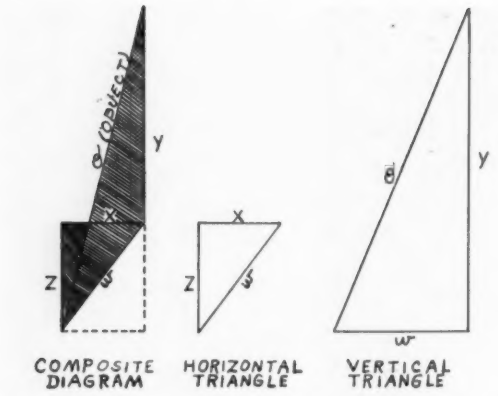

FIG. 4. Basic geometric figures involved with a nonhorizontal object occupying three dimensions in space.

(3) Therefore,

$$\frac{X_1}{D_1}=\frac{X_1+s}{D_1+s+d_1}$$

(4) Simplified, $X_1(s+d_1)=sD_1$
(5) And,

$$X_1=\frac{sD_1}{s+d_1}$$

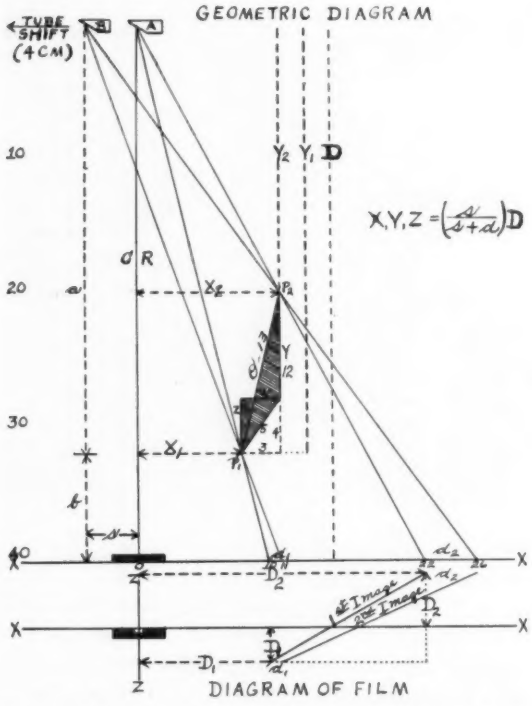

FIG. 5. Diagram for nonhorizontal diameters. Note that the two images on the film diagram are unequal and that the two displacements are not equidistant.

(6) Similarly,

$$X_2=\frac{sD_2}{s+d_2};\quad Z_1=\frac{sD_1}{s+d_1}\quad Z_2=\frac{sD_2}{s+d_2}$$

Solving for the Y components

(1) $$\frac{s}{d_1}=\frac{a}{b}$$

(2) $sb=d_1a$
But $a=Y_1$ and $b=D_1-Y_1$
(3) Substituting for "a" and "b" in equation (2)
$s(D_1-Y_1)=d_1Y_1$
(4) Simplified, $sD_1=Y_1(s+d_1)$
(5) And

$$Y_1=\frac{sD_1}{s+d_1}$$

(6) Similarly,

$$Y_2=\frac{sD_2}{s+d_2}$$

However, for each end of the image,

$$\frac{s}{s+d}$$

is a constant factor which represents the corrective factor for distortion. In order to facilitate computations this should be computed first. Then equations (5) and (6) may be expressed as:

$$X,\ Y \text{ or } Z=\left(\frac{s}{s+d}\right)D$$

From this diagram we note:

X Coordinates	*Z Coordinates*	*Displacements*
$D_1=10$ cm.	$D_1=2.5$ cm.	$d_1=11-10=1$ cm.
$D_2=22$ cm.	$D_2=4.0$ cm.	$d_2=26-22=4$ cm.

Since:

$$\frac{s}{s+d_1}=\frac{4}{4+1}=0.8 \quad \text{and} \quad \frac{s}{s+d_2}=\frac{4}{4+4}=0.5$$

Then substituting in the general formula for the components of the three axes:

$$X_1=0.8\times 10 = 8 \text{ cm.}$$
$$Y_1=0.8\times 40 = 32 \text{ cm.}$$
$$Z_1=0.8\times 2.5 = 2 \text{ cm.}$$
$$X_2=0.5\times 22 = 11 \text{ cm.}$$
$$Y_2=0.5\times 40 = 20 \text{ cm.}$$
$$Z_2=0.5\times 4 = 2 \text{ cm.}$$

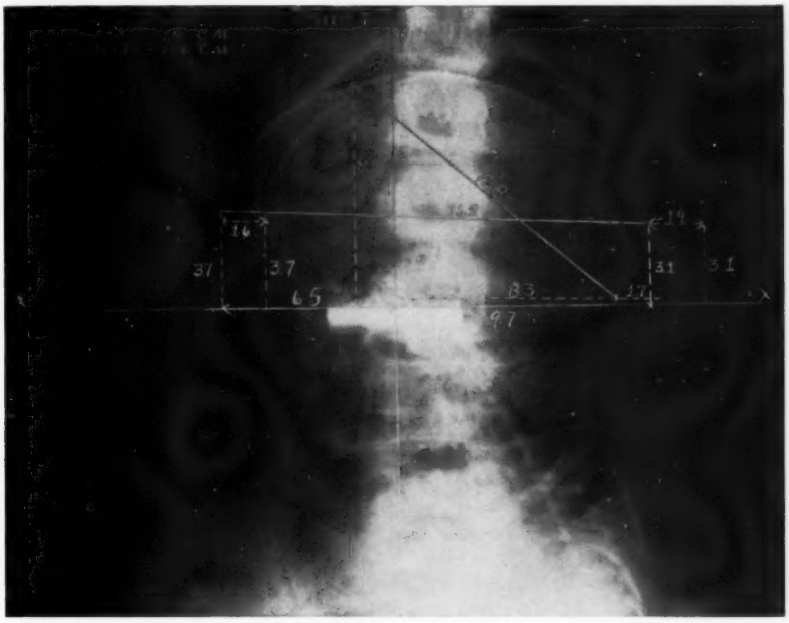

FIG. 6. Nonhorizontal diameters in cephalometry with breech presentation. Both exposures made on the same film.

The two components of the Y axis must always be subtracted from each other.

The two components of the X or Z axis must either be added together or subtracted from each other. This can be determined by the relation of the first exposure image to the X and Z axes. A right angle triangle is completed by lines drawn from each end of this image which forms the hypotenuse of the triangle. If the two components of an axis lie on the same side of the other axis these components are subtracted; if they lie on opposite sides, they are added (Fig. 5).

Thus:

$$X = X_2 - X_1 = 11 - 8 = 3 \text{ cm.}$$
$$Y = Y_1 - Y_2 = 32 - 20 = 12 \text{ cm.}$$
$$Z = Z_1 + Z_2 = 2 + 2 = 4 \text{ cm.}$$

And since:

$$O = \sqrt{X^2 + Y^2 + Z^2}$$

Then:

$$O = \sqrt{(3)^2 + (12)^2 + (4)^2} = \sqrt{169} = 13 \text{ cm.}$$

Figure 6 shows a breech presentation with unequal displacements indicating nonhorizontal diameters. The tube shift and target-film distance were 5 and 100 cm., respectively.

Measurements and solutions obtained were as follows:

1. *Occipitofrontal Diameter*

X Coordinates	*Z Coordinates*	*Displacements*
$D_1 = 6.5$ cm.	$D_1 = 3.7$ cm.	$d_1 = 1.6$ cm.
$D_2 = 9.7$ cm.	$D_2 = 3.1$ cm.	$d_2 = 1.9$ cm.

Solution: $O = 12.6$ cm.
Post natal measurement—12.7 cm.

2. *Suboccipitobregmatic Diameter*

Z Coordinates	*Z Coordinates*	*Displacements*
$D_1 = 1.5$ cm.	$D_1 = 8.5$ cm.	$d_1 = 1.5$ cm.
$D_2 = 8.3$ cm.	$D_2 = 0.3$ cm.	$d_2 = 1.7$ cm.

Solution: $O = 10.11$ cm.
Post natal measurement—10.0 cm.

Solution of Suboccipitobregmatic Diameter by Proportion. The displacement at the bregma may be difficult to visualize. However, both the occipitofrontal and suboccipitobregmatic diameters can be measured easily In Figure 6 these diameters measured 16.2 and 12.8 cm., respectively. Since both of these diameters lie in the sagittal plane, the suboccipitobregmatic diameter can be determined by a direct proportion, after the occipitofrontal diameter has been computed by the general formula.

Therefore:

$$\frac{16.2}{12.8} = \frac{12.6}{O}$$
$$O = 9.95 \text{ cm.}$$

Figures 7 and 8 represent the same fetus in head presentation. Two exposures were made in each oblique position, using separate films for each exposure. The tube shift and target-film distance were 6 and 100 cm., respectively. Quasifrontal and lateral views of the fetal head were obtained.

Measurements and solutions were as follows:

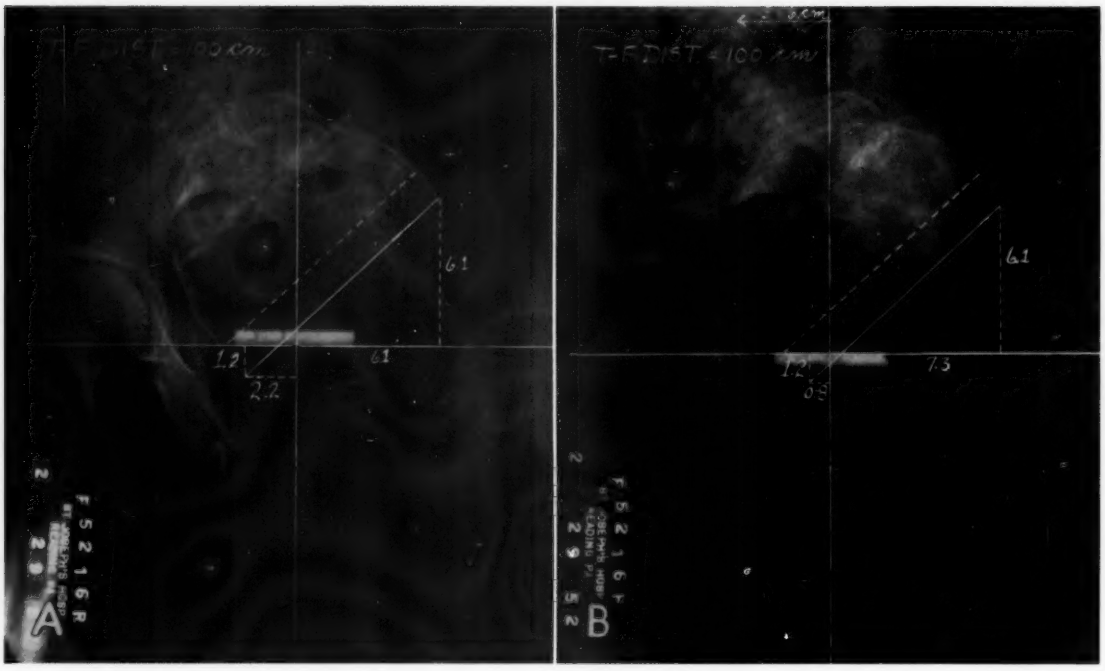

FIG. 7. (*A*) and (*B*). Nonhorizontal diameter in cephalometry with head presentation. Exposures made on separate films with the patient in right posterior oblique position. The biparietal diameter is drawn parallel to the dotted supraorbital diameter. The second cassette (*B*) was inadvertently used upside down but the notch in the marker indicates the true axial lines.

1. *Biparietal Diameter*

X Coordinates	*Z Coordinates*	*Displacements*
$D_1 = 2.2$ cm.	$D_1 = 1.2$ cm.	$d_1 = 1.4$ cm.
$D_2 = 6.1$ cm.	$D_2 = 6.1$ cm.	$d_2 = 1.2$ cm.

Solution: $O = 9.43$ cm.
Postnatal measurement—9.4 cm.

2. *Occipitofrontal Diameter*

X Coordinates	*Z Coordinates*	*Displacements*
$D_1 = 5.9$ cm.	$D_1 = 1.0$ cm.	$d_1 = 1.1$ cm.
$D_2 = 6.1$ cm.	$D_2 = 4.0$ cm.	$d_2 = 1.3$ cm.

Solution: $O = 11.0$ cm.
Postnatal measurement—11.2 cm.

3. *Suboccipitobregmatic Diameter*

X Coordinates	*Z Coordinates*	*Displacements*
$D_1 = 2.6$ cm.	$D_1 = 4.2$ cm.	$d_1 = 1.1$ cm.
$D_2 = 0.7$ cm.	$D_2 = 6.2$ cm.	$d_2 = 1.3$ cm.

Solution: $O = 9.35$ cm.

The occipitofrontal and suboccipitobregmatic diameters measure 13 and 11 cm., respectively. Solution by proportion:

$$\frac{13}{11} = \frac{11.05}{O}$$

Solution: $O = 9.35$ cm.
Postnatal measurement—9.3 cm.

The different diameters of the fetal head in utero usually lie from about 10 to 35 cm. above the film. If the target-film and the tube shift distances are standardized, a table of correction factors will simplify computations. The range of the table can be easily determined. For instance; with target-film and tube shift distances of 100 and 5 cm. respectively, the displacements will be from about 0.5 to 3 cm., since $10/90 \times 5 = 0.55$ cm. and $35/65 \times 5 = 2.7$ cm. Such a table would appear as shown at the top of the next page.

COMMENT

A variety of problems have been presented dealing with measurements involving one, two or three dimensions of space. It is realized that in frontal pelvimetry, the Thoms' perforated plate described by Torpin, Holmes and Hamilton[7] and by Henderson[2] is more desirable since this method requires only one exposure. Similarly, the isometric method described by McLane[5] and others is preferred for lateral pelvimetry. However, I have presented the different aspects of pelvicephalometry as

CORRECTION FACTOR TABLE

Target-Film Distance—100 cm.		Tube Shift—5 cm.	
Displacements (cm.)	*Correction Factors* $\left(\frac{s}{s+d}\right)^2$	*Displacements (cm.)*	*Correction Factors*
0.5	0.909	1.8	0.735
0.6	0.893	1.9	0.724
0.7	0.877	2.0	0.713
0.8	0.862	2.1	0.703
0.9	0.847	2.2	0.694
1.0	0.833	2.3	0.684
1.1	0.819	2.4	0.675
1.2	0.806	2.5	0.666
1.3	0.793	2.6	0.657
1.4	0.781	2.7	0.649
1.5	0.769	2.8	0.641
1.6	0.757	2.9	0.633
1.7	0.746	3.0	0.625

proof of the general application of this method and for better comprehension of the basic principles involved.

I believe that this method may have its greatest value in cephalometry. Ball[1] expressed the circumference of the fetal skull in terms of volume. Scarpellino[6] states that, because of rotation and position of the fetal head, linear measurements of the head are difficult to obtain accurately. Obviously, the more rotation and obliquity of the fetal head, the less accurate are the linear measurements when the method used presupposes that the fetal head lies only in one plane.

The author's method takes all three dimensions of space into consideration. Moderate rotation of the fetal head will not interfere with accurate computations. However, extreme rotation of the head might interfere with visualization of the proper linear measurements.

SUMMARY

A simple general formula is presented for computations in pelvicephalometry provided that the two extreme points of a part to be measured can be visualized.

The basic portion of this formula is the correction factor which can be determined by this method regardless at what level the part to be computed lies. The formula for this factor is simple and constant for all types of problems.

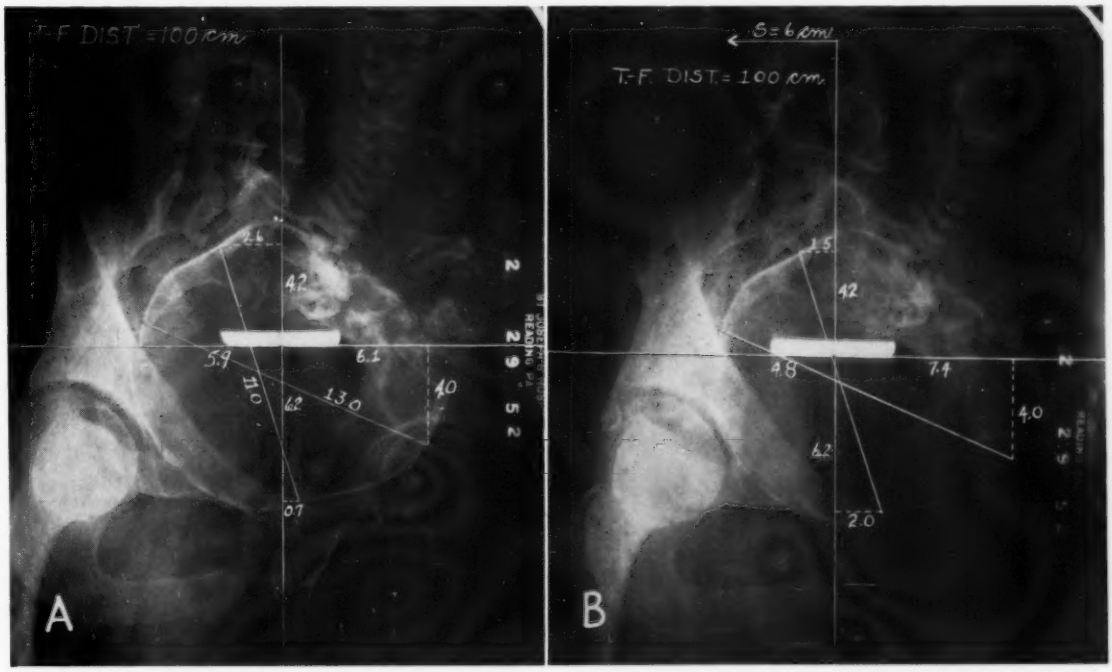

FIG. 8. (*A*) and (*B*). Nonhorizontal diameters in cephalometry of same fetus as in Figure 7. Exposures made on separate films with the patient in left posterior oblique position.

In cases of horizontal diameters, this factor is applied directly to the diameters of either image for computing the actual diameters.

In cases of nonhorizontal diameters the correction factors are applied to the coordinates of the three axes of the first exposure image. In these cases there will be two correction factors: one for each end of the part to be computed.

The simplicity of the formula and technique and its general application renders this method of practical use.

This method also offers a means for localization. The Y components of this formula denote the distance at which an anatomical part or foreign body lies from the target.

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ROENTGEN PARALYSIS IN THE MOUSE*

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INTRODUCTION

IT IS a well known fact that the most radioresistant cells are those which are most highly differentiated and which are incapable of dividing (Bergonié and Tribondeau[2]). Accordingly, the central and peripheral nervous systems of adult animals are extremely resistant to roentgen irradiation (Obersteiner;[21] Bagg;[1] Rieder and Rosenthal;[22] Mogilnitzky and Podljaschuk;[20] Meissel;[19] Zimmern and Chavany;[34] Lyman, Kupalov and Scholz;[18] Clark;[8] Warren;[31] Ellinger;[10,11] Janzen and Warren;[15] Warren;[32] Campbell, Peterson and Novick;[6] Bloom;[3] and others). But the embryonic nervous tissue is one of the most sensitive to roentgen rays (Schmidt;[28] Caspari;[7] Kosaka;[16] Demel;[9] Gladstone and Colwell;[13] Scholz;[29] Mogilnitzky and Podljaschuk;[20] Rugh;[24,25,26] Wilson;[33] Hicks;[14] and others). The problem arises as to when the very sensitive embryonic nervous tissue acquires the radioresistance of the adult nervous tissue. According to Scheremetjewa and Brunst,[27] the spinal cords of young tadpoles of *Pelobates fuscus* (prior to the development of limb anlagen) have not shown any changes after treatment with 3,750–7,500 roentgens and are, therefore, very radioresistant. However, young axolotls (*Siredon mexicanum*) irradiated with 5,000 r, one month after hatching (without posterior limb anlagen but with anterior limbs), have radiosensitive spinal cords (Brunst[5]). In the treated region of these animals, the spinal cord in many specimens was completely destroyed. As a result of this, a complete paralysis of the posterior limbs and tail was observed in many cases. The young axolotls used in the latter experiments had a body form similar to that of the adult, and they had anterior limbs, while the tadpoles used in the first mentioned experiments (Scheremetjewa and Brunst[27]) had no limbs at all. In spite of the more advanced development of the axolotls, their spinal cords maintain the "embryonal" sensitivity to roentgen rays, while the spinal cords of tadpoles show adult radioresistance.

The central nervous system of adult mice is very radioresistant. According to the observations of Figge (unpublished), irradiation of parts of the central nervous system of adult mice with tremendous doses (20,000 r) had no effect upon the structure of the treated nervous tissue or upon the behavior of these animals. What, then, is the reaction of the spinal cord to local irradiation in young mice? Consideration of this problem is the purpose of this paper.

MATERIAL AND METHOD

In this investigation, 268 mice of the C_{57} (Black) strain were used. The mice were irradiated at the age of 1, 2, 3, 4, 5, 6, 10, 15, 20, and 25 days. Certain difficulties were encountered in attempts to irradiate such young animals. After treatment of the young, some mothers ate the entire litter or refused to feed their young. Many treated mice died at various times after irradiation, and results could not be obtained. Especially large mortality was observed after irradiation of very young animals* (see Fig. 1).

Litter mates were used as experimental groups in the present investigation. In each group, the animals were irradiated with 3,400–4,000 r. Only some mice, at the age of 25 days, were irradiated with 5,000 r. The small mice were immobilized during treatment by means of strips of adhesive tape. They were so placed beneath the localizer slit of the protective lead cover that only a narrow band (4

* The high mortality of mice 6 days old probably is accidental. The number of animals in this experiment is small.

* This work was supported by grants from the National Cancer Institute of the United States Public Health Service.

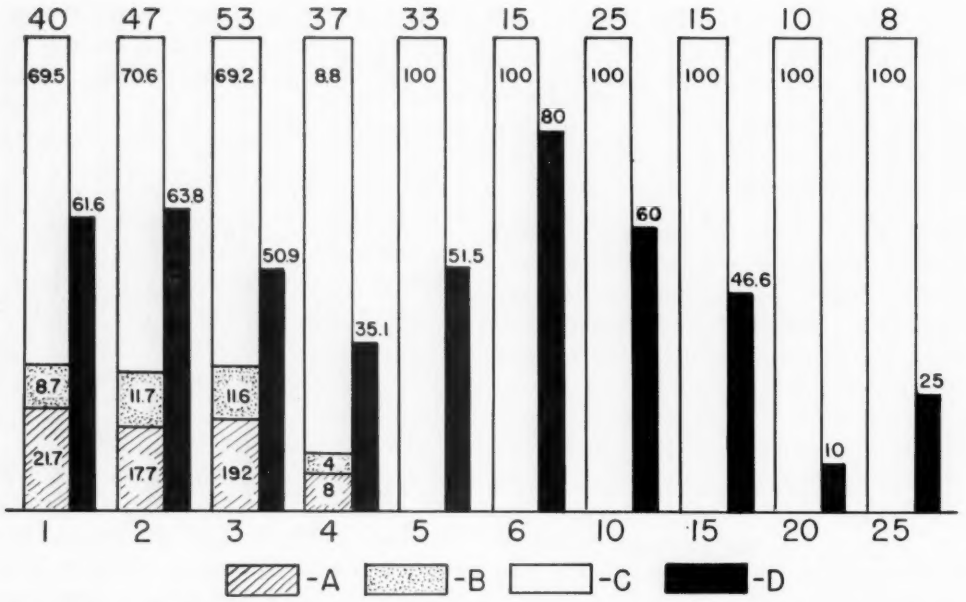


FIG. 1. Comparison of effects of local roentgen irradiation of part of the bodies (midway between the fore and hind limbs) of mice of various ages. Figures above the large columns are numbers of irradiated animals of one age; figures below the large columns are the ages of animals in days. Figures above the solid black columns are the percentages of animals which died at various times after irradiation and not included in results. *A* (diagonal lines), animals with complete paralysis; *B* (stipple), animals with partial paralysis; *C* (blank), animals with normal behavior; *D* (solid black), animals which died.

mm. wide) midway between the fore and hind limbs was irradiated. The irradiation of these mice was carried out under the following conditions: 55 kv. max., 3 ma., no filter; the target-object distance was 12 cm.

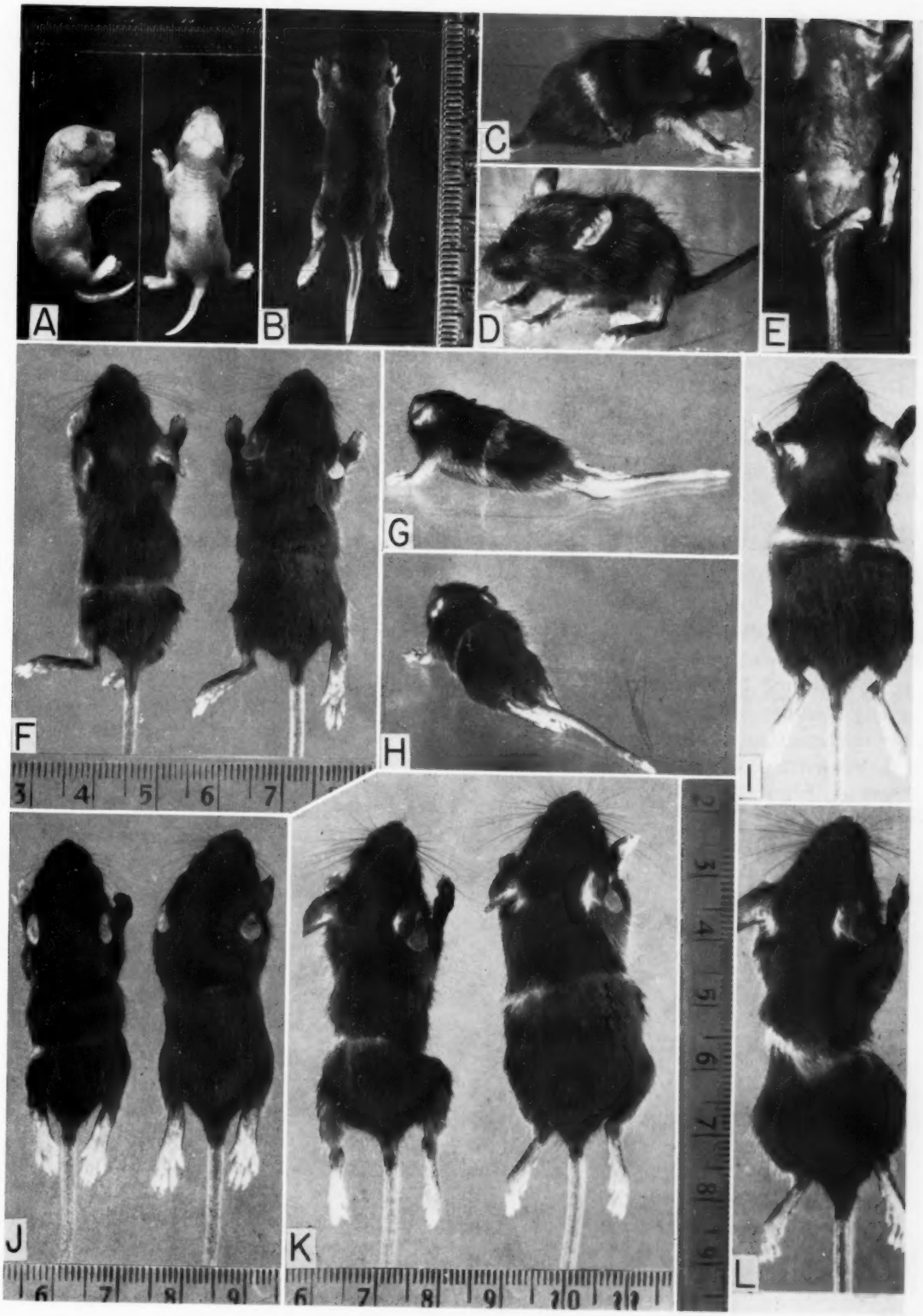
The experimental mice were under observation for many months and in some cases, for more than one year. The fixations of paralyzed animals were made by means of a saturated solution of bichloride of mercury with 5 percent acetic and with Zenker with acetic acid. The fixed material was embedded in paraffin and transverse sections were made at 10 microns. The sections were stained with Ehrlich's hematoxylin and eosin.

RESULTS

Irradiation of mice of various ages shows that a paralysis is never observed following roentgen irradiation of mice at the ages of 5, 6, 7, 10, 15, 20, or 25 days, but after irradiation of mice 1–4 days old, paralysis was seen in some cases (Fig. 1). It was observed in some experimental groups that gradual development of paralysis occurred. In one such group, examined 19 days after treatment, some of the treated mice showed temporary disturbances of the movements of the posterior parts of

⟿

FIG. 2. Effect of local roentgen irradiation of part of the bodies (midway between the fore and hind limbs) of mice of various ages. (*A*) one day old normal mouse; (*B*) five day old normal mouse; (*C*) (*D*) (*E*) various views of a nonnarcotized 20 day old mouse (irradiated at age of 1 day) with a partial paralysis of the right hind limb; (*F*) comparison of a 20 day old mouse with partial paralysis (left) and a mouse from the same litter with complete paralysis (right) irradiated at the age of 1 day; (*G*) (*H*) nonnarcotized 17 day old mouse with complete paralysis irradiated at the age of 2 days: (*I*) 25 day old mouse without paralysis, irradiated at age of 2 days; (*J*) comparison of 16 day old mouse with complete paralysis (left) and mouse from the same litter without paralysis (right) irradiated at age of 1 day; (*K*) comparison of 21 day old mouse with complete paralysis (left) and mouse from the same litter without paralysis (right) irradiated at the age of 1 day; (*L*) 30 day old mouse without paralysis (irradiated at the age of 3 days).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the body. In such mice, following a period in which normal movements were observed, there occurred a sudden partial paralysis of the hind limbs. This paralysis persisted for several seconds and then completely disappeared. After a time, the paralysis was observed again. This state may be termed a "temporary intermittent paralysis" and is the first sign of the permanent paralysis which eventually follows. After 11 days (30 days after treatment), some mice showed a permanent paralysis of the posterior limbs, hind part of the body, and the tail. These parts did not react to any form of irritation. It should be noted that in some of the paralyzed animals, occasional movements of the tail could be observed, but these movements were erratic and were not correlated with other activities of the animal. The paralyzed mice crept by using the anterior limbs only (Fig. 2,*G*,*H*). The paralysis was not complete in all cases. In some animals, only one hind limb was paralyzed; in others, the entire posterior part of the body was affected, including the limbs and tail, but the paralysis was incomplete and occasional movements of the limbs or tail could be observed. Figure 2 (*C*, *D*, *E* and *F*—left) shows various views of a nonnarcotized mouse that had a partial paralysis of the right hind limb. As a result of the paralysis, the limb is abnormal in position. Paralysis was observed at 19 days after treatment. It is interesting to note that paralysis, when it occurred, was always observed 15–30 days after irradiation.

The question arises why only some mice were paralyzed, while the others had normal motion and sensitivity (Fig. 1). A possible explanation of this is that paralysis was observed only in animals which were irradiated exactly in the region of the motor neurons controlling the hind limbs. The photographs of treated mice with paralysis (Fig. 2, *F*-left, partial paralysis; *F*-right, complete paralysis; *J* and *K*-left, complete paralysis) and without paralysis (Fig. 2, *I*, *J*, and *K*-right and Fig. 2, *L*) show that all mice without paralysis were irradiated in a more rostral region than the mice which were paralyzed. The difference in positions of the irradiated regions of mice with partial and complete paralysis is shown in Figure 2, F. In cases when mice were irradiated in more caudal regions than the region of motor neurons controlling the hind limbs, the paralysis was also not observed.

Several other authors have described some paralytic symptoms, convulsive movements, and other small disturbances of locomotion in irradiated animals (Rodet and Bertin-Sans,[23] Krukenberg,[17] Walter,[30] Brunner,[4] Gabriel,[12] and others); but I did not find any work which described complete paralysis as a result of roentgen irradiation.

Histopathological examination showed that, in most cases, the appearance of the spinal cord of the irradiated mouse with complete paralysis is normal and cannot be distinguished from the spinal cord of a control mouse. The appearance of the nerve in a paralyzed limb is also normal. The general conclusion is that the damage of the spinal cord after local roentgen irradiation cannot be demonstrated in most cases by histopathological examination. Obviously, the damage occurs only in some cells of the spinal cord, and such a type of damage is very difficult to establish by the usual histopathological examination.

However, in some cases (comparatively very rare), the damage of the spinal cord is evident. For example, one animal was fixed about 8 months after treatment. During this period, there was observed a complete paralysis of the entire posterior part of the body. Figure 3 shows drawings made form transverse sections through the spinal cord and axial skeleton (shown in contours only). These drawings were all made at the same magnification by means of the camera lucida. The figures show that the spinal cord was almost completely destroyed in the treated region. The growth of certain elements of the axial skeleton was suppressed (compare

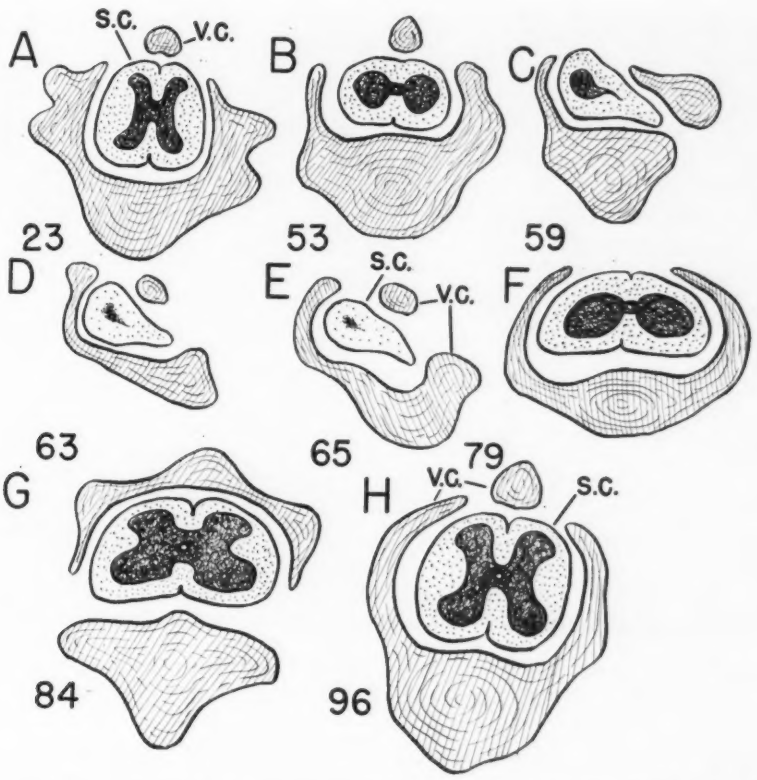

Fig. 3. Transverse sections through the spinal cord and vertebral column of an animal 8 months after irradiation with 3,400 r. All semischematic drawings were made at the same magnification with the aid of a camera lucida. The figures 23, 53, etc., slide numbers; s.c. spinal cord; v.c., elements of vertebral column.

D and *E* with *A* and *H* in Fig. 1). It is noteworthy that the spinal cord in the untreated region is completely normal in appearance. It was found that the caudal part of the spinal cord, although isolated for a long period of time from the more cranial parts of the central nervous system by the damaged area of the cord, was alive and had a normal appearance. In spite of this, changes not easily detected must have occurred. The same observation was described in the axolotl (Brunst[5]). Here, the caudal portion of the spinal cord, completely isolated from the other parts of the central nervous system, remained alive and had a histological structure which appeared normal.

Some of the paralyzed mice can survive for a very long period of time. For example, the paralyzed mouse shown in Figure 4,*A* lived for 10 months following irradiation of the middle portion of the body with 3,400 r. In the roentgenogram of this mouse (Fig. 4,*B*), the treated region was easily distinguished because the vertebral column in this region was especially thin (obviously a result of growth suppression). The pronounced curvature of the vertebral column in the treated region was evidently a result of the weakness of the affected portion of the column and its inability to withstand muscular forces exerted upon it (Fig. 4,*B*). Histopathological investigation disclosed that the spinal cord of this animal was completely destroyed in the treated region.

It is to be emphasized that the treated mouse, in spite of its paralysis, was able to live so long. Obviously the digestive organs, etc., continuued to function well enough to support the life of these animals. The spinal cord and vertebral column of

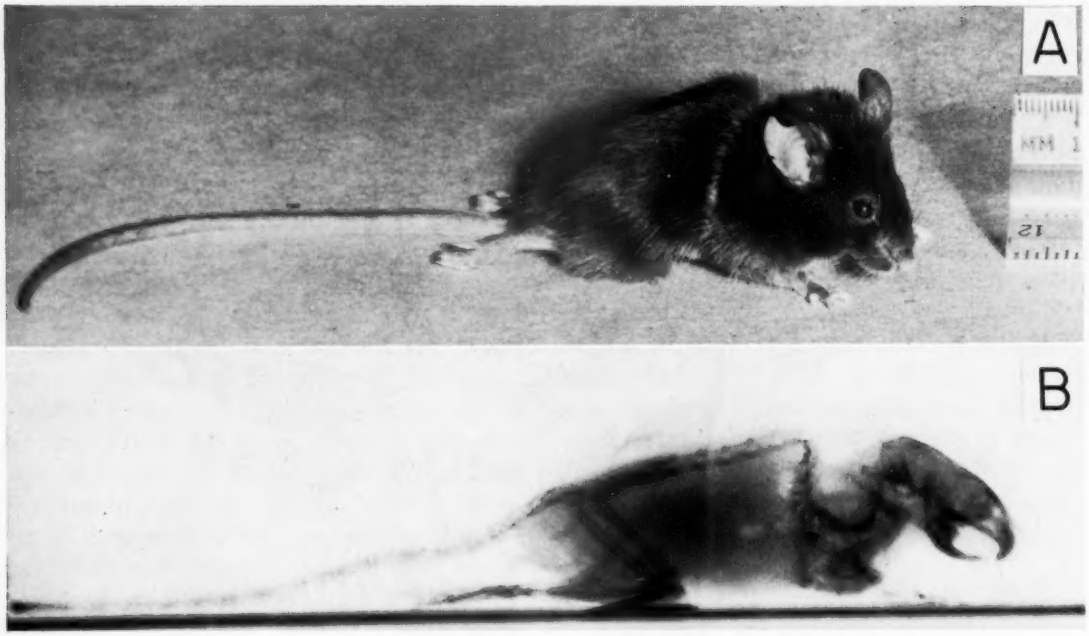

FIG. 4 (*A*) Photograph of a mouse with complete paralysis 10 months after irradiation of the middle part of the body with 3,400 r. (*B*) Roentgenogram of the same mouse.

the treated region were the only parts to show distinct damage as the result of irradiation. In addition to these deeper effects, there was noted a temporary suppression of hair growth and a change from the normal hair color to gray (Fig. 4,*A*).

Both of the cases described above are important, because complete paralysis caudal to the irradiated regions was observed in these animals, in spite of the fact that the irradiation was not made in the lumbar region but in the chest region. This is especially well shown in the roentgenogram of the mouse (Fig. 4,*B*). Possibly the destruction of the spinal cord in these cases is secondary to the suppression of growth and partial resorption of the vertebral column. Obiously, in these cases, the complete interruption of the spinal cord in the irradiated region provokes secondary changes which involve the function of the motor neurons in the lumbar region and, as a result of this, complete paralysis occurs.

Some of the greatest changes during development of a mouse occur during the first week of life after birth. The change in roentgen sensitivity of the spinal cord occurs approximately between 4 and 5 postpartum days. The great difference in appearance of mice 1 and 5 days old is clear from the photographs (Fig. 2,*A* and *B*). A 1 day old mouse resembles an embryo and a 5 day old mouse more closely resembles an adult organism. During this time, the neurons of the lumbar region of the spinal cord change from cells which are relatively sensitive to roentgen irradiation to the more resistant status of the more adult form.

SUMMARY

The bodies of 268 mice at the age of 1, 2, 3, 4, 5, 6, 10, 15, 20, and 25 days were irradiated with 3,400–5,000 roentgens midway between the fore and hind limbs through a localizer slit 4 mm. in width. A paralysis is never observed following roentgen irradiation of mice at the ages of 5–25 days. But after irradiation of mice 1–4 days old, paralysis was seen in some cases. This paralysis was observed usually in animals which were irradiated exactly in the region

of the motor neurons controlling the hind limbs.

Histopathological examination showed that in most cases the appearance of the spinal cord of the paralyzed mice is normal. Obviously, the damage occurs only in some cells of the spinal cord and is very difficult to detect by the usual histopathological examination. However, in some cases, the damage of the spinal cord is evident. In these animals, irradiation was made in the chest region, and complete interruption of the spinal cord probably is the result of weakness (suppression of growth) of the affected portion of the vertebral column. This interruption provokes the secondary alteration of the function of motor neurons in the lumbar region and, as a result of this, complete paralysis occurs.

The change in roentgen sensitivity of the spinal cord occurs approximately between 4 and 5 days after birth. At this time, the neurons controlling the hind limb transformed from cells relatively sensitive to roentgen rays to the more resistant status of the adult form.

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Vol. 71, No. 1

RECOMMENDATIONS OF THE INTERNATIONAL COMMISSION ON RADIOLOGICAL UNITS

REVISED AT THE SEVENTH INTERNATIONAL CONGRESS OF RADIOLOGY, COPENHAGEN, DENMARK, JULY, 1953

I. DEFINITIONS AND UNITS

1. *Intensity of radiation* is the energy flowing through unit area perpendicular to the beam per unit time. It is expressed in ergs per square centimeter per second or watts per square centimeter.

2. *Quantity of radiation* is the time integral of intensity. It is the total energy which has passed through unit area perpendicular to the beam and is expressed in ergs per square centimeter or watt-seconds per square centimeter.

3. *Absorbed dose* of any ionizing radiation is the amount of energy imparted to matter by ionizing particles per unit mass of irradiated material at the place of interest. It shall be expressed in *rads*.

4. The *rad* is the unit of absorbed dose and is 100 ergs per gram.

5. Inasmuch as calorimetric methods of determining absorbed dose are not usually practicable, ionization methods are generally employed. The quantity which must be measured is the ionization produced in a gas by the same flow of corpuscular radiation as exists in the material under consideration. The energy, E_m, imparted to unit mass of the material is then essentially related to the ionization per unit mass of gas, J_m, by the equation

$$E_m = W S J_m$$

where W is the average energy expended by the ionizing particles per ion pair formed in the gas, and S is the ratio of the mass stopping power of the material to that of the gas.

6. Since the calculation of the absorbed dose from measurements of ionization requires a knowledge of the parameters W and S as well as variables characterizing the radiation and the irradiated material, it is recommended that tables of the best available data be prepared and held under continual review.*

7. The roentgen (r) remains the unit of X- and γ-ray dose and its definition remains unchanged as below:

> *The roentgen* shall be the quantity of X- or γ-radiation such that the associated corpuscular emission per 0.001293 gram of air produces, in air, ions carrying 1 electrostatic unit of quantity of electricity of either sign.

8. It becomes increasingly difficult to measure the dose in roentgens as the quantum energy of the X- or γ-radiation approaches very high values. The unit may, however, be used for most practical purposes for quantum energies up to 3 mev.

9 *Integral absorbed dose* is the integration of the energy absorbed throughout a given region of interest. The unit is the *gram-rad*. 1 gram-rad = 100 ergs.

10. Amounts of radioactive material shall be expressed in curies. The accepted definition of the curie is:

> *The curie* is a unit of radioactivity defined as the quantity of any radioactive nuclide in which the number of disintegrations per second is 3.700×10^{10}.

With this definition the curie is independent of the disintegration rate of radium.

11. It is suggested that the γ-ray emission be expressed in terms of roentgens per millicurie-hour at 1 cm. from a point source. This quantity is different for every isotope. Preliminary data have been compiled relating to a number of radioactive isotopes and will be supplemented from time to time.*

12. The International Commission on Radiological Units requests the national standardizing laboratories to set up, inter-

* Preliminary reports on this subject were presented to the Commission and it is hoped will be published in the near future.

change and compare standards of X-rays, γ-rays and radioactive isotopes, maintain close contact with each other, and generally by every means within their power further the improvement of methods of standardization.

II. SPECIFICATION OF RADIATION TREATMENT

13. The specification of the conditions of radiation treatment should be such as to enable the treatment to be reproduced in all its essential features. The completeness of dose estimations, in roentgens or rads, will vary in practice, but all specifications should be as detailed as possible.

A. *Beam therapy.*

(1) The nature of the beam may be conveniently characterized by stating the following factors:

(i) The type of beam used, e.g., X-rays, radium, cobalt-60, cesium-137, neutron, electron, etc.

(ii) The peak voltage or the energy of the gamma radiation.

(iii) The inherent and added filter.

(iv) For X-rays the half-value layer in some material such as:

Aluminum	(10 to 120 kv.)
Copper	(120 to 400 kv.)
Tin or lead	(400 kv. to 1 mv.)
Lead	(Above 1 mv.)

(2) In the recording of technique and dosage the following considerations should be included:

(i) The number, dimensions, and location of the parts of radiation.

(ii) The source-to-skin distance.

(iii) The time interval between successive treatments.

(iv) The number of treatments given.

(v) The total time over which a course of treatment is spread.

(vi) The dose-rate at some suitable point and the time of each treatment.

(vii) Any two of the following factors should be recorded:

(1) Air dose.
(2) Backscatter factor.
(3) Skin dose, for each irradiation.

For beam radiations with energies greater than 1 mev. and for rotation therapy other factors may be substituted.

(viii) The nature and method of use of "bolus" material.

(ix) Depth-dose values at appropriate points along the axis should be specified.

(x) Total tissue-dose determinations and calculations should be made as complete as possible.

At least the following total doses, in rads or roentgens, should be stated:

(a) Maximum skin dose.
(b) Maximum dose in irradiated tissue.
(c) Maximum dose in tissue of interest or tumor.
(d) Minimum dose in tissue of interest or tumor.

B. *Surface, intracavitary, and interstitial use of radioactive substances.*

(1) The description of the treatment should be given in sufficient detail to permit duplication of the technique.

(2) The physical characteristics of the radioactive material should be given including half-life and type and energy of radiations emitted.

(3) The nature and thickness of material traversed by the radiation before reaching the tissues should be stated.

(4) The amount of radioactive ma-

terial in millicuries and the total millicurie-hours should be stated.

(5) The number of applications and spacing.

(6) The total time of the treatment.

(7) The total dose delivered to appropriate points of interest within the tissues.

C. *Systemic treatment by radioactive isotopes.*

(1) The technique of administration should be given in sufficient detail to permit duplication.

(2) The physical and chemical nature of the radioactive isotope should be stated, including half-life and type and energy or radiations emitted.

(3) The amount of radioactive material in millicuries should be stated.

(4) The effective half-life and the pattern of distribution in tissues of interest should be given as completely as possible.

III. RULES GOVERNING THE SELECTION AND WORK OF THE INTERNATIONAL COMMISSION ON RADIOLOGICAL UNITS

14. (a) The International Commission on Radiological Units (ICRU) shall be composed of a chairman and not more than twelve other members. The selection of members shall be made by the International Executive Committee (IEC) from a list of nominations submitted by the national delegations and by the ICRU itself. Members of the ICRU shall be chosen on the basis of their recognized activity in the field of radiological units and standards, without regard to nationality.

(b) The ICRU shall be composed of at least three medical radiologists and three physicists.

(c) The members of the ICRU shall be selected during one International Congress to serve through the succeeding Congress. Not less than two but more not than four members of the ICRU shall be changed at any one Congress. In the intervening period of vacancy caused by conditions beyond the control of the IEC shall be filled on the recommendation of the ICRU.

(d) In the event of a member of the ICRU being unable to attend the ICRU meetings, a substitute may be selected by the ICRU as a temporary replacement. Such a substitute member shall not have voting privileges at the meetings unless specifically authorized by the IEC.

(e) The ICRU shall be permitted to invite individuals to attend its meetings to give special technical advice. Such persons shall not have voting privileges, but may ask permission to have their opinions recorded in the minutes.

15. The continuance of the record of the ICRU shall be in the hands of a secretary of the ICRU, elected by the ICRU from among its regular members and subject to the approval of the IEC.

16. The ICRU shall familiarize itself with progress in the whole field of radiation units and standards. The secretary shall be responsible for the preparation of a program to be submitted to the Commission for discussion at its meetings. Preliminary reports shall be prepared and circularized to all members of the ICRU and other specially qualified individuals at least six months before the meeting of the Congress.

17. The Chairman shall be elected by the ICRU during one International Congress to serve through the succeeding Congress. The choice shall not be limited to the country in which it is proposed to hold the succeeding Congress.

18. Decisions of the ICRU shall be decided by a majority vote, with the chairman casting the deciding vote in a case of a tie. A minority opinion may be appended to the minutes of a meeting if so desired by any member and upon his submission of same in writing to the secretary.

IV. SUBCOMMITTEES

19. The Commission has established two

Subcommittees, on (1) X-ray standards, and (2) standards of radioactive isotopes.

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Thirty-sixth Annual Meeting: The Homestead, Hot Springs, Virginia, March 14, 15 and 16, 1954.

EDITORIAL

THE THIRTY-SIXTH ANNUAL MEETING OF THE AMERICAN RADIUM SOCIETY

THE Thirty-sixth Annual Meeting of the American Radium Society will be held at The Homestead, Hot Springs, Virginia, on Sunday, Monday and Tuesday, March 14, 15 and 16, 1954. Everyone interested in therapeutic radiology is cordially invited to attend. The program, published in this issue of the JOURNAL, holds something of interest for everyone concerned in the treatment of patients with malignant disease, as well as for those particularly engaged with the more recent developments in the isotope and supervoltage field.

The Sunday afternoon session, arranged by Dr. Richard H. Chamberlain, will consist of step-by-step carrying out of procedures in the several problems to be demonstrated. For the isotope cases, the counting equipment will be functioning; for the roentgen-ray and radium cases, localizing films, beam directing devices, and other accessories will be employed. Ample time will be available for questioning the demonstrators. This should be a most interesting and instructive program.

The two topics selected for symposia are among the most important in cancer therapy today. Cancer of the lung is apparently on the increase, and results of treatment are not encouraging. Progress can be made only by interdisciplinary coordination. Four speakers, each an expert in his part of the field, should give a broad picture and a start for good general discussion. Lesions in the nasopharynx are a challenge to the therapeutic radiologist. Many are dissatisfied with their own procedures, but have not as yet been able to decide how best to improve them. Panel members will consider first the treatment of a definite case by four quite different procedures. Following a critical analysis of the four by other panel members, the essayists and the moderator hope for lively discussion from the floor.

The Janeway Lecture will be presented by Dr. Lauriston S. Taylor, Chief of the Atomic and Radiation Physics Division, National Bureau of Standards, on the subject of Education in Radiation Safety. Nobody has worked longer or more persistently in this field. The topic is especially timely because of new recommendations adopted at the Seventh International Congress of Radiology.

Individual presentations on such varied subjects as treatment of malignant disease in children, the use of radioactive gold in pelvic tumors and of neutrons in brain lesions, the relation of the doctor and the cancer patient, and several others, complete an unusually varied program.

There will be a cocktail party Sunday evening. The Janeway Lecture will be presented at a luncheon on Monday, and on that evening the annual banquet of the Society will be held.

Since the American Radium Society decided to meet at a time and place of its own choosing, instead of immediately preceding the American Medical Association, it has been possible to select pleasant places. Hot Springs, in the early spring, should be delightful. The hotel offers excellent indoor and outdoor recreational facilities. The scientific program will not be so crowded that all enjoyment of these is precluded, and many who attend may wish to spend an additional day or two relaxing in comfortable surroundings. The Society, with its relatively small membership, has a reputa-

tion for friendliness and good-will, as well as for high professional standing. We hope that all the members will come and maintain this tradition, so that our guests will in turn want to become members.

Reservations should be arranged directly with The Homestead, Hot Springs, Virginia, mentioning that they are for the meeting of the American Radium Society. All members have received mimeographed information regarding transportation, accommodations, registration, and so forth, and others desirous of attending can obtain this from the Secretary of the Society, Dr. Robert E. Fricke, Mayo Clinic, Rochester, Minn.

Edith H. Quimby
President, American Radium Society
College of Physicians and Surgeons
New York, New York

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Shoreham Hotel, Washington, D.C., Sept. 21–24, 1954.

AMERICAN RADIUM SOCIETY
Secretary, Dr. R. E. Fricke, Mayo Clinic, Rochester, Minn. Annual meeting: The Homestead, Hot Springs, Virginia, March 14–16, 1954.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y. Annual meeting: 1954, to be announced.

AMERICAN COLLEGE OF RADIOLOGY
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich. Annual meeting: 1954, to be announced.

FIFTH INTER-AMERICAN CONGRESS OF RADIOLOGY
General Secretary, Dr. Eugene P. Pendergrass, 3400 Spruce St., Philadelphia 4, Pa. Meets at Shoreham Hotel, Washington, D. C., April 24–30, 1955.

ALABAMA RADIOLOGICAL SOCIETY
Secretary, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

ARIZONA RADIOLOGICAL SOCIETY
Secretary, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

ATLANTA RADIOLOGICAL SOCIETY
Secretary, Dr. Albert A. Rayle, Jr., 478 Peachtree St., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. J. J. Daversa, 345 75th St., Brooklyn, N.Y. Meets monthly fourth Tuesday, October through April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. Elbert K. Lewis, 6337 S. Harvard Ave., Chicago, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. Mortimer Lubert, 10515 Carnegie Ave., Cleveland 6, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

COLORADO RADIOLOGICAL SOCIETY
Secretary, Dr. Parker Allen, Children's Hospital, Denver, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

CONNECTICUT VALLEY RADIOLOGIC SOCIETY
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday October and April.

DALLAS-FORT WORTH ROENTGEN STUDY CLUB
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. F. Lang, Harper Hospital, Detroit, Mich. Meets monthly first Thursday, October to May, at Wayne County Medical Society Building.

EAST BAY ROENTGEN SOCIETY
Secretary, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. H. G. Reaves, Medical Arts Bldg., Sarasota, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. Robert M. Tankesley, 218 Doctors Bldg., Atlanta, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

GREATER MIAMI RADIOLOGICAL SOCIETY
Secretary, Dr. E. H. Bryson, 273 Alhambra Circle, Coral Gables, Fla. Meets third Wednesday of each month at Veterans Administration Building.

HOUSTON RADIOLOGICAL SOCIETY
Secretary, Dr. Harry Fishbein, 324 Medical Arts Bldg., Houston 2, Texas. Meets fourth Monday each month at Hermann Hospital.

IDAHO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Alfred M. Stone, St. Lukes Hospital, Boise, Idaho. Meets annually at same time as Idaho State Medical Association.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Stephen L. Casper, 1101 Maine St., Quincy, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

IOWA RADIOLOGICAL SOCIETY
Secretary, Dr. James T. McMillan, 1104 Bankers Trust Bldg., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

KANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Willis L. Beeler, M.D., 700 Kansas Ave., Topeka, Kansas. Meets in spring with State Medical Society, and in winter on call.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

KINGS COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. Solomon Maranov, 1450 51st St., Brooklyn 19, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

LOS ANGELES RADIOLOGICAL SOCIETY
Secretary, Dr. George Jacobson, 1200 N. State St., Los Angeles 33, Calif. Meets second Wednesday each month at Los Angeles County Medical Association Building, Los Angeles.

* Secretaries of societies are requested to send timely information promptly to the Editor.

Maine Radiological Society
Secretary, Dr. Hugh Allan Smith, Eastern Maine General Hospital, Bangor, Maine. Meets in early spring, June and fall.

Maryland Radiological Society
Secretary-Treasurer, Dr. H. Leonard Warres, 2337 Eutaw Place, Baltimore 17, Maryland.

Miami Valley Radiological Society
Secretary, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

Mid-Hudson Radiological Society
Secretary, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, September to May.

Milwaukee Roentgen Ray Society
Secretary, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. John R. Hodgson, Mayo Clinic, Rochester, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

Mississippi Radiological Society
Secretary, Dr. John W. Evans, 117 N. President St., Jackson, Miss. Meets third Thursday of each month at the Rotisserie Restaurant at 6:30 P.M.

Montana Radiological Society
Secretary, Dr. Grant P. Raitt, Suite 413 Medical Arts Bldg., Billings, Montana. Will meet at least once a year.

Nassau Radiological Society
Secretary, Dr. Frank Huber, Hempstead, N. Y. Meets second Tuesday of the month in February, April, June, October and December.

Nebraska Radiological Society
Secretary, Dr. J. F. Kelly, Jr., 816 Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. Stanley M. Wyman, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Harvard Club.

New Hampshire Roentgen Ray Society
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

New York Roentgen Society
Secretary, Dr. J. R. Freid, 1049 Park Ave., New York 28, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Radiological Society
Secretary, Dr. W. C. Sternbergh, Charlotte Memorial Hospital, Charlotte, N. C. Meets in May and October.

North Dakota Radiological Society
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement.

Northeastern New York Radiological Society
Secretary, Dr. D. H. Baxter, Albany Hospital, Albany, N. Y. Meets in Albany area on second Wednesdays of October, November, March and April.

Northern California Radiological Society
Secretary, Dr. H. B. Stewart, 2920 Capitol Ave., Sacramento, Calif. Meets at dinner last Monday of each month, September to June.

Ohio State Radiological Society
Secretary, Dr. M. M. Thompson, 316 Michigan St. Toledo, Ohio.

Oklahoma State Radiological Society
Secretary, Dr. John R. Danstrom, Medical Arts Bldg., Oklahoma City, Okla. Three regular meetings annually.

Oregon Radiological Society
Secretary, Dr. J. W. Loomis, 919 Taylor St. Bldg., Portland 5, Oregon. Meets monthly from October to June on the second Wednesday of each month at 8:00 P.M. at the University Club.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

Pacific Northwest Radiological Society
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. J. M. Converse 416 Pine St., Williamsport. Next annual meeting at Bedford Springs Hotel, Bedford, Penna., May 14 and 15, 1954.

Philadelphia Roentgen Ray Society
Secretary, Dr. H. M. Stauffer, Temple University Hospital, Philadelphia 40, Pa. Meets first Thursday of each month, at 5 P.M., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. Donald H. Rice, Western Pennsylvania Hospital, Pittsburgh 24, Pa. Meets 6:00 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

Radiological Section, Baltimore Medical Society
Secretary, Dr. H. Leonard Warres, 2337 Eutaw Place, Baltimore 17, Md. Meets third Tuesday each month, September to May, inclusive.

Radiological Section, Connecticut Medical Society
Secretary, Dr. William A. Goodrich, 85 Jefferson St., Hartford 6, Conn. Meetings are held bi-monthly.

Radiological Section, Medical Society of the District of Columbia
Secretary, Dr. A. C. Wyman, 5445—28th St., N.W., Washington, D. C. Meets Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Radiological Society of Greater Cincinnati
Secretary, Dr. Chapin Hawley, 927 Carew Tower, Cincinnati 2, Ohio. Meets monthly from September to June on first Monday of each month at 7:30 P.M. at the Cincinnati General Hospital.

Radiological Society of Hawaii
Secretary, Dr. P. S. Arthur, Young Hotel Bldg., Honolulu 13, T. H. Meets third Friday of each month at a place designated by the Secretary.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of Louisiana
Secretary, Dr. J. T. Brierre, 700 Audubon Bldg., New Orleans. Meets annually during Louisiana State Medical Society Meeting.

Radiological Society of New Jersey
Secretary, Dr. Salomon Silvera, 921 Bergen Ave., Jersey City, N. J. Meets at Atlantic City at time of State Medical Society and in November in Newark, N. J.

Radiological Society of Southern California
Secretary, Dr. Donald R. Laing, 65 N. Madison Ave. Pasadena 1, Calif.

Richmond County Radiological Society
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. A. Gordon Ide, 277 Alexander St., Rochester 7, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. John H. Freed, 4200 East Ninth St., Denver 7, Colo.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. Francis O. Trotter, Jr., 634 N. Grand Blvd., St. Louis 3, Mo. Meets fourth Wednesday each month, except June, July, August and September.

SAN ANTONIO-MILITARY RADIOLOGICAL SOCIETY
Secretary, Dr. Hugo F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets Brook Army Medical Center Officers Mess first Monday of each month.

SAN DIEGO RADIOLOGICAL SOCIETY
Secretary, Dr. C. W. Bruner, 2456 Fourth Ave., San Diego 1, Calif. Meets first Wednesday of each month at the University Club.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary, Dr. I. J. Miller, 2680 Ocean Avenue, San Francisco 27, Calif. Meets quarterly.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. H. R. Morris, 1027 "D" St., San Bernardino, Calif.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. George E. Irwin, Jr., 703 N. East St., Bloomington, Ill.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOUTH BAY RADIOLOGICAL SOCIETY
Secretary, Dr. W. H. Graham, 634 East Santa Clara St., San Jose 12, Calif. Meets second Wednesday each month.

SOUTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. William A. Klauber, Self Memorial Hospital, Greenwood, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. G. K. Henshall, 311 Medical Arts Bldg., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort worth 4, Texas. Next meeting, Dallas, Texas, Jan. 29 and 30, 1954.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May, Service Memorial Institute.

UTAH STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

VIRGINIA RADIOLOGICAL SOCIETY
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY
Secretary, Dr. John N. Burkey, 555 Medical-Dental Bldg., Seattle 1, Wash. Meets fourth Monday of each month from September through May.

WEST VIRGINIA RADIOLOGICAL SOCIETY
Secretary, Dr. W. Paul Elkin, 515 Medical Arts Bldg., Charleston, W. Va. Meets concurrently with annual meeting of West Virginia State Medical Society; other meetings arranged by program committee.

WESTCHESTER RADIOLOGICAL SOCIETY
Secretary, Dr. C. G. Huntington, 170 Maple Ave., White Plains, N. Y. Meets on third Tuesdays of January and October and on two other dates.

WISCONSIN RADIOLOGICAL SOCIETY
Secretary, Dr. W. W. Moir, 309 Geele Ave., Sheboygan, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-RAY STUDY CLUB OF SAN FRANCISCO
Secretary, Dr. Wm. W. Saunders, Veterans Administration Hospital, San Francisco 21, Calif. Meets monthly, third Thursday, at 7:45 P.M., Lane Hall, Stanford University Hospital.

CUBA, MEXICO, PUERTO RICO AND CENTRAL AMERICA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

SOCIEDAD MEXICANA DE RADIOLOGIA Y FISIOTERAPIA
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA
Secretary, Dr. Rafael A. Blanes, Ave. Ponce de Leon 1175, Santurce, P. R.

SOCIEDAD RADIOLÓGICA PANAMEÑA
Secretary, Dr. L. Arrieta Sanchez, Apartado No. 86, Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

FACULTY OF RADIOLOGISTS
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

CANADIAN ASSOCIATION OF RADIOLOGISTS
Honorary Secretary-Treasurer, Dr. D. L. McRae, Suite 305, 1555 Summerhill Avenue, Montreal 25, Que. Meetings January and June.

SECTION OF RADIOLOGY, CANADIAN MEDICAL ASSOCIATION
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

COLLEGE OF RADIOLOGISTS (AUSTRALIA AND NEW ZEALAND)
Honorary Secretary, Dr. Alan R. Colwell, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W.

SOUTH AMERICA

ASOCIACION ARGENTINA DE RADIOLOGIA
Secretary, Dr. Lidio G. Mocsa, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, JUNTA CENTRAL, BUENOS AIRES
Secretary, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL LITORAL, SEDE, ROSARIO
President, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL SUR, SEDE, LA PLATA
President, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL CENTRO SEDE, CORDOBA
President, Prof. Dr. David L. Caro, Corro 86, Cordoba. Meets monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL NORTE, SEDE, TUCUMAN
President, Dr. Julio Mendez Valladares, Rivadavia 358, Tucuman. Meets monthly.

Sociedad Argentina de Radiologia, Filial de Cuyo Sede, Mendoza.
President, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Colombiana de Radiologia
Secretary, Dr. Luis E. Lozano B., Carrera 12 No. 20–69, 6º piso, Bogota, Colombia. Meets last Thursday of each month.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Société Française d'Electro-Radiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord
Secretary-General, Dr. A. Dariaux, 9 bis, Boulevard Rochechouart, Paris IXe, France.

Ceskoslovensk společnost pro rëntgenologii a Radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept., Akademia Gdansk.

Wrocław Section Polish Society of Radiology
Secretary, Dr. R. Marciniak, Akad. Medyczna Wrocław, 68 Curie-Skłodowska St., Wrocław, Poland. Meets first Sunday of each month, X-Ray Department, Akademia Medyczna Wrocław.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

Deutsche Roentgen-Gesellschaft
Secretary, Dr. Peter Kröker, (22a) Essen-Helsingen, Westpreussenstrasse 21. Meets annually in different towns.

Societa Italiana di Radiologia Medica
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

India

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

AMERICAN RADIUM SOCIETY

PRELIMINARY PROGRAM

THE following is the tentative program which has been arranged by the Program Committee under the chairmanship of the President, Dr. Edith H. Quimby, for the Thirty-sixth Annual Meeting of the American Radium Society to be held at The Homestead, Hot Springs, Virginia, Sunday, Monday and Tuesday, March 14, 15 and 16, 1954.

Sunday, March 14, 1954
Opening Session: 2:00–5:00 P.M.

Convening of Meeting

Welcoming Remarks. M. B. Jarman, M.D., Hot Springs, Va.

Presidential Address. Edith H. Quimby, Sc.D., New York, N. Y.

Demonstration of Radiological Procedures. Richard H. Chamberlain, Philadelphia, Pa., "Producer." Assisted by Theodore P. Eberhard, M.D., Morton M. Kligerman, M.D., Robert Robbins, M.D., James Bierly, B.A., Robert Gorson, B.A., John Hale, B.A., and Jean Meszaros, B.A.

Monday, March 15, 1954
Morning Session: 9:00 A.M.–12:00 M.

Symposium: Cancer of the Lung. Paul E. Rekers, M.D., Los Angeles, Calif., Moderator.

- Pathology. Samuel H. Rosen, M.D., Washington, D. C.
- Surgery. John L. Pool, M.D., New York, N. Y.
- Conventional X-ray Therapy. Theodore P. Eberhard, M.D., Philadelphia, Pa.
- Supervoltage Therapy. Thomas Watson, M.D.

Effect of Two-Million Volt Therapy on Various Types of Malignant Tumors in the Upper Abdomen. Ruth J. Guttman, M.D., Jamaica, N. Y.

Planned Combination of Surgery and Radiation in Treatment of Advanced Primary Head and Neck Cancer. William S. MacComb, M.D., and Gilbert H. Fletcher, M.D., Houston, Texas.

Dermatological Problems in the Practice of Radiology. Jesshill Love, M.D., Louisville, Ky.

Luncheon Session: 12:15–2:15 P.M.

The Janeway Lecture: Education in Radiation Protection.

Lauriston S. Taylor, Ph.D., Chief, Atomic and Radiation Physics Division, National Bureau of Standards, Washington, D. C.

Afternoon Session: 2:30–4:00 P.M.

The Doctor and the Cancer Patient. Lowell S. Goin, M.D., Los Angeles, Calif.

The Value of an Interdisciplinary Approach to Clinical Cancer. Alfred Gellhorn, M.D.

Considerations in the Use of Ionizing Radiation in Children. Harold W. Dargeon, M.D., New York, N. Y.

Radiotherapy in Pediatrics. Ralph F. Phillips, M.D., New York, N. Y.

Annual Banquet: 7:00 P.M.

Tuesday, March 16, 1954
Morning Session: 9:00A.M.–12:00 M.

Symposium: Treatment of Nasopharyngeal Neoplasms.

- Douglas Quick, M.D., New York, N. Y., Moderator.
- Conventional X-ray Therapy. H. B. Elkins, M.D., Iowa City, Iowa.
- Beam Directed X-ray Therapy Supplemented by Radium. Clifford L. Ash, M.D., Toronto, Ontario.
- Rotation Therapy at Conventional Voltages. Robert Robbins, M.D., Philadelphia, Pa.
- Supervoltage Therapy. James W. F. Carpender, M.D., Chicago, Ill.
- Critical Summaries. Isadore Lampe, M.D., Ann Arbor, Mich., and Robert J. Bloor, M.D., Rochester, N. Y.

Clinical Application of the Paterson-Parker System in Interstitial Radium Therapy. Fernando G. Bloedorn, M.D., Houston, Texas.

Nomographic Wheel for 3-Dimensional Localization of Radium Sources and Calculation of Dose Rate. J. G. Holt, A.B.

Radium Accidents: Emergency and Decontamination Techniques. Robert G. Gallagher, M.D., and Eugene L. Saenger, M.D., Cincinnati, Ohio.

Afternoon Session: 2:00–4:00 P.M.

Slow Neutron Depth Dose Measurements. E. E. Stickley, Ph.D., Upton, Long Island, N. Y.

Some Factors Influencing Radiation Skin Damage. G. Failla, Sc.D., New York, N. Y.

The Therapeutic Effects of Single Doses of Total Body Radiation. Vincent P. Collins, M.D., Houston, Texas.

Radiation Dosimetry in the Treatment of Carcinoma of the Cervix with Radioactive Colloidal Gold. Michel Ter-Pogossian, Ph.D., Alfred I. Sherman, M.D., and Willard Allen, M.D., St. Louis, Mo.

The Results of Radiation Therapy for Recurrent Cancer of the Cervix. Martin Van Herik, M.D., and Robert E. Fricke, M.D., Rochester, Minn.

SIXTH ANNUAL MID-WINTER RADIOLOGICAL CONFERENCE

The Sixth Annual Mid-Winter Radiological Conference, sponsored by the Los Angeles Radiological Society, will be held at the Ambassador Hotel, Los Angeles, California, on Saturday and Sunday, February 20 and 21, 1954. A banquet preceded by cocktails will be held at the Ambassador Hotel on Saturday evening, February 20.

The out-of-state speakers will be Dr. Eugene P. Pendergrass, Philadelphia, Pennsylvania, Dr. U. V. Portmann, Tucson, Arizona, Dr. Marcy L. Sussman, Phoenix, Arizona, and Dr. Frederic E. Templeton, Seattle, Washington.

Hotel reservations should be made as soon as possible through the Convention Manager, Ambassador Hotel, Los Angeles.

Conference reservations may be made through Dr. Harold P. Tompkins, 658 South Westlake Avenue, Los Angeles 57, California. The Conference fee is $20.00, and the dinner will be $7.50 per plate. Courtesy cards for the Conference are available to radiological residents and radiologists in military service by pre-registration.

EASTERN CONFERENCE OF RADIOLOGISTS

The Section on Radiology of the Medical Society of the District of Columbia will be host to the Eastern Conference of Radiologists at its 1954 session. The meeting will take place at the Statler Hotel, Washington, D. C., on Friday and Saturday, March 12 and 13, 1954. Registration will begin on Thursday afternoon, March 11.

Hotel reservations should be made at the Statler as soon as possible.

The constituent organizations of the Conference are The New England Roentgen Ray Society, The New York Roentgen Ray Society, The Philadelphia Roentgen Ray Society and the radiological sections of the Medical Society of Baltimore City and of the District of Columbia Medical Society. The annual session rotates among the five member groups.

An interesting program has been arranged and will include a visit to the newly activated National Institutes of Health. Information concerning the meeting may be obtained from Dr. Karl C. Corley, Chairman, Committee on Arrangements, 1835 Eye St., N. W., Washington 6, D. C.

COLORADO RADIOLOGICAL SOCIETY

At the October, 1953, meeting the Colorado Radiological Society elected the following officers: *President*, Dr. William Curtis, Boulder; *Vice President*, Dr. Raymond Lanier, Denver; *Secretary*, Dr. Parker Allen, Children's Hospital, Denver; *Treasurer*, Dr. Thomas Kennedy, Denver.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA

The first meeting of the newly formed Radiological Society of Southern California was held at the Huntington Hotel, Pasadena, California, on October 17, 1953. Dr. Lyell C. Kinney of San Diego is the *President* of the Society and Dr. Donald R. Laing, 65 North Madison Avenue, Pasadena 1, California, the *Secretary-Treasurer*. Dr. James T. Case of Santa Barbara, Dr. Lowell S. Goin and Dr. John D. Camp of Los Angeles, along with the officers, constitute the *Board of Directors*.

ANNOUNCING A NEW JOURNAL

Plans have been completed for the publication of a new journal, *Radiation Research*, as the official organ of the Radiation Research Society. Dr. Titus C. Evans, College of Medicine, State University of Iowa, is the Managing Editor of the new periodical. The Editorial Board includes fifteen Associate Editors selected from outstanding universities and research centers. Dr. H. J. Curtis and Dr. A. Edelmann, both of Brookhaven National Laboratory, and Dr. G. Failla of Columbia Uni-

versity constitute the Executive Committee of the Board of Editors.

Radiation Research will publish original articles dealing with all phases of radiation research to promote the integration of the disciplines of physics, chemistry, biology, and medical research as they are concerned with the effects of radiation on matter. The term "radiation" is here used in its broadest sense and specifically includes ionizing, ultraviolet, infrared, and visible radiations. The journal will help physicists, chemists, biologists, and medical researchers to keep abreast of new developments in a rapidly expanding field that has numerous ramifications and a widely scattered literature.

The new journal is to be published bimonthly, with six issues to a volume. Number 1 of Volume 1 is scheduled for release in February, 1954. Among the papers to be published in the early issues are a group devoted to radiation chemistry, radiation biology and medical research, and a Symposium on Physical Measurements in Radiobiology.

Radiation Research will be published by the Academic Press, 125 East 23rd St., New York 10, New York.

POSTGRADUATE COURSE IN ORTHOPEDICS

A two-week Postgraduate Course in Orthopedic Diagnosis and Treatment will be given by the Hospital for Joint Diseases, under the auspices of Columbia University College of Physicians and Surgeons at the Hospital for Joint Diseases, New York, New York, March 15 through 27, 1954. Fee for the course is $100. The class will be limited to 20 students. The course will run for two weeks Monday through Friday 9 A.M. and 4 P.M., Saturday 9 A.M. to 12 noon.

Application blanks may be obtained from Associate Dean, Postgraduate Instruction, Columbia University College of Physicians and Surgeons, 630 West 168 Street, New York, 32, New York.

DEUTSCHE RÖNTGEN-GESELLSCHAFT

The Deutsche Röntgen-Gesellschaft, at its thirty-fifth meeting in Stuttgart, named Professor W. Baensch, of Washington, D. C., Professor C. Gauss, Bad Kissingen, and Dr. B. Hauff, Stuttgart, as Honorary Members of the society in recognition of their great services to roentgenology.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

Einführung in die Enzephalographie (Pneumenzephalographie). Von Dr. med. habil. Otto Schiersmann, Dozent für Neurologie und Psychiatrie, Chefarzt des Krankenhauses Bethesda, Wuppertal-Elberfeld. Cloth. Price, DM 36.–. Pp. 135, with 186 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1952.

This monograph is meant and written as an introduction to air studies of the brain. Both encephalography and ventriculography are included. Approximately half of the book is devoted to the description of the normal findings, whereas the remainder of the text contains a short description of pathological processes. The first chapter of the monograph describes the anatomy of the ventricular system and of the subarachnoidal space, the second the dynamics and mechanics of the spinal fluid. The third chapter discusses the air filling in a general way in regard to the point of introduction of air, distribution of air, resorption of air, influence of small amounts of air and observation of the pressure during the injection and sequelae of air injection. The fourth chapter describes the technique, the fifth the interpretation of the normal encephalogram and ventriculogram. The sixth chapter gives a short general description of the pathological processes. The seventh is devoted to the borderline of normal and pathological encephalogram, while the last chapter describes the appearance of the encephalogram in various pathological processes.

The general part of the monograph is of interest and will give the beginner a good review of the advantages and disadvantages of various methods and of the underlying principles. The special part is—in accordance with the purposes of this book—rather short.

The author has used the German literature quite extensively, and has made a not always completely successful attempt to make use of the foreign literature.

The illustrations are large and very satisfactory. The printing is excellent.

The monograph is a good introduction to encephalography and ventriculography. The experienced examiner may find some helpful hints in regard to the presentation of his material for teaching purposes.

Richard Schatzki, M.D.

Clinical Dental Roentgenology. Technic and Interpretation. Including Roentgen Studies of the Child and the Adolescent. By John Oppie McCall, D.D.S., F.A.C.D., Former Director, The Murry and Leonie Guggenheim Dental Clinic, etc.; and Samuel Stanley Wald, D.D.S., F.A.C.D., Clinical Professor of Oral Cancer and Roentgenology, New York University College of Dentistry, etc. Third edition. Cloth. Price, $8.50. Pp. 384, with 475 illustrations. W. B. Saunders Company, West Washington Square, Philadelphia, Pennsylvania, 1952.

This is the third edition of the book which was published originally in 1940. It presents first a complete but concise description of the technique for the production and processing of intraoral and extraoral films. In addition to the standard intraoral technique, the use of the long cone is discussed. The more commonly used extraoral views of the facial bones and mandible are described as well as the cephalometric technique. In the chapter on time of exposure of the films, very definite consideration is given to protection of both the patient and operator. This is a factor too frequently disregarded in the use of the roentgen ray. The chapter dealing with the darkroom, its accessories and processing of the films, is excellent and includes tabulation of the causes of faulty roentgenograms. The section of the book devoted to technique is concluded with a description of the routine complete intraoral survey for both the child and adult and a short chapter on stereoscopic roentgenography.

The remaining chapters of the book are given to interpretation. A few pertinent rules for interpretation are mentioned and the authors point out that an oral diagnosis should not be based on the roentgenographic examination alone but must include the information obtained from the patient's history, tests for vi-

tality and thorough clinical examination. The normal roentgenographic appearance of the teeth and supporting tissues begins with the prenatal period and follows through infancy and preadolescence to maturity. Then the appearance of the normal anatomical landmarks of the jaws are described with particular reference to the intraoral films. Following this, the abnormalities of development and the variations in growth and eruption are considered. The remaining chapters are devoted to interpretation of pathological conditions occurring in and about the teeth and jaws.

The entire book is well illustrated and the text is complete but concise. This is a book which can be well recommended to both the student and practitioner of dental roentgenology.

Haven F. Doane, D.D.S.

La colangiografia laparoscopia (colangiografia no quirurgica). Por M. Royer. Paper. Pp. 172, with 79 illustrations. Librería "El Ateneo" Editorial, Florida 340, Buenos Aires, Argentina, 1952.

This monograph summarizes the author's work and experience of several years with a technique of cholangiography by puncture of the gallbladder through the abdominal wall, with the help of peritoneoscopy. The instruments and the technique are described in detail. A summary of physiological observations in the experimental animal as well as in man is given, together with references to the author's work in this field. There are numerous reproductions of roentgenograms showing lithiasis, inflammatory conditions and tumors. The principal inconvenience seems to result from the peritoneal irritation caused by spilling of the contrast medium after the procedure; this is obviated by emptying the gallbladder after the examination is completed. In 440 cases no fatalities resulted. Technical errors and pathologic conditions accounted for failures in one-fourth of the attempts. The procedure is contraindicated in acute or subacute conditions.

There is an English summary at the end of the most important chapters and bibliographic references of pertinent works by other authors are also given. All those interested in the special subject of the monograph will find very valuable information, honest discussion of the limitations of the procedure and an interesting example of original work excellently presented.

J. A. del Regato, M.D.

Röntgenuroskopie. Nierenbecken und -kelche, Harnleiter, Blase, Harnröhre. Von Dr. med. habil. G. W. Günther, Mannheim. Paper. Price, DM 13.50. Pp. 45, with 86 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1952.

The author of this small book applies methods of modern gastrointestinal roentgenology with detailed mucosal pattern studies to the problems of urology; in preference to static pyelography he employs systematically roentgenoscopy with intermittent spot-filming under suitable conditions of rotation and compression and with the patient in various positions, from the Trendelenburg to the erect position. The author is quite familiar with analogous work by Manges, Legueu, Fey and Truchot, and others, and discusses in detail problems proposed by Bogard who tried to clarify distress symptoms on functional basis when no anatomic basis for disease could be discovered. The author is aware of the unphysiologic approach of his procedure realizing that cinematography in conjunction with excretory urography might yield different answers.

Particular discussion is devoted to problems of vascular impressions and constricting sulci, which might alter the mucosal pattern of the kidney on thin layer filling; a vascular etiology of painful states of otherwise normal renal pelves and ureters is denied. It is stated that vascular crossings of normal sized renal and ureteral lumina are not demonstrable roentgenologically. The knowledge of marginal overshadowing effects of various structures is advantageous in interpretation of spot films. Loop formation of ureters cannot be attributed to blood vessel crossings. They are regarded as the effects of tonus, inspiration and expiration and of the mechanics of forced retrograde filling of the lumina. Hypertonicity and spasmophilia may produce temporarily many confusing and misleading images. Small semi-opaque and non-opaque calculi may be demonstrated much more reliably by careful spot-filming with thin layer filling of the urinary passages. Similarly, valuable information can be obtained in regard to the urinary bladder and the urethra as, for instance, in the study of diverticula and strictures.

The roentgen uroscopic method is regarded as far superior to "blind" pyelography, though the author warns against unjustified overenthusiasm and emphasizes that not all pain

referable to the renal pelvis can be symbolized pyelographically; occurrence and frequency of painful states of the upper urinary passages of nervous origin requires further study and clarification, which may not be obtainable by roentgenologic methods.

The reviewer doubts that many American urologists and radiologists can be persuaded to do such painstaking work. They might become familiar with this method and employ it occasionally, though much of its value may be lost unless it is practiced regularly and meticulously. There are 86 excellent illustrations showing the value of the roentgen uroscopic method as applied to the various segments of the urinary passages and the problems under study.

Hans A. Jarre, M.D.

Die Frühdiagnose des Uteruscarcinoms. Histologie, Kolposkopie, Cytologie, biochemische Methoden. Von Prof. Dr. Med. Hans Limburg, Oberarzt an der Universitäts-Frauenklinik, Hamburg. Zweite verbesserte Auflage. Cloth. Price, DM 19.50. Pp. 208, with 83 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1952.

The second edition of the monograph of about two hundred pages reports on the experience with the large material of the Gynecological Clinic of the University of Hamburg in the field of diagnosis of uterine cancer in its early stages. The main theme is the methods of diagnosis for the so-called carcinoma in situ. A new chapter on biochemical methods has been added. Detailed studies and statistics lead to the conclusion that the cytological diagnosis should not be overvalued and that the other methods (colposcopy with biopsy, etc.) must remain the basis of early diagnosis of cancer of the uterus. The Papanicolaou method gave 6.2 per cent false positive results in 5,970 examinations. Many excellent photomicrographs are reproduced illustrating the findings.

The book should be of great interest to gynecologists and radiotherapists and to pathologists who are concerned with the earliest possible diagnosis of cancer of the uterus.

Hans W. Hefke, M.D.

Lésions nouvelles du poignet. Pseudokystes nécrobiotiques. Kystes par herniations capsulaires. Arthrite chronique dégénérative par ostéochondrose marginale. Acta radiologica, Supplement 90. Par Jean-Pierre Bugnion. Paper. Price, Sw. Kr. 20:–. Pp. 123, with numerous illustrations. Acta radiologica, Stockholm 2, Sweden, 1952.

For more than fifty years radiologists have been interested in the lacunar shadows often found in the bones of the wrist. Kienböck's discovery of semilunar malacia drew attention to the bony changes in this part of the skeleton. There have been descriptions of "cysts" or "cystoid lesions," which various authors have attributed to trauma, rupture of connective tissue attachments carrying nutrient vessels, or even fracture or infraction of the damaged bone. Anomalies have also been mentioned but no one has offered any precise explanation. Generally they are without symptoms and thus escape the attention of the clinicians. The author has undertaken a systematic study of the subject.

The first part of the report is based on six hundred roentgenograms of the wrist from autopsy material of the Geneva Institute of Pathology, during a period of six months. More than half of the wrists as examined (305) showed lacunar images, often bilateral, and generally affecting several bones of the same wrist. Right wrist involvement was more common than the left. There was no relation to sex or profession or occupation. The frequency increased with age, the maximum occurring between sixty-one and seventy years.

The second part reports the histopathologic examination of eighteen of the roentgenologically most interesting wrists. The histology and pathogenesis of the bony changes led to exclusion of the overstrain hypothesis. Cysts were found to develop as the result of herniation of the synovial membrane into the bone; or they occurred as necrobiotic pseudocysts, due to vascular disturbances; or they were of the arthrotic marginal types.

The *hernial cysts* imply the existence of a site of lessened resistance constituted by the insertion of the ligaments and the penetration of the blood vessels. These cysts were not larger than 2 or 3 millimeters in diameter, corresponding to the lacunar form of young subjects.

The *necrobiotic type* develops on the basis of vascular disturbances. The cysts, measuring as much as 8 or 10 or more millimeters, occur especially in the aged. It often coexists with the hernial form.

The *marginal arthrotic type* raises many problems, some not yet solved. They include car-

tilaginous lesions secondary to the presence of cystic formation beneath the articular cartilage. Or there may be an elective involvement of the osseous tissues called marginal laminar osteochondrosis, which may terminate in bony fusion. It is the result of ischemic disturbances.

James T. Case, M.D.

Die Osteomalazie. Von Dr. Med. Markus Wernly, Bern. Paper. Price, DM 14.40. Pp. 101, with 16 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1952.

This is a monograph of 101 pages in which the author discusses the various aspects of osteomalacia. Included are chapters on the etiology, pathology, clinical diagnosis and therapy of the disease. Illustrations of the roentgen findings are included in the sixteen reproductions. Particular attention is given to late or adolescent rickets and the osteomalacia occurring in females. An extensive bibliography of 208 references is appended.

L. W. Paul, M.D.

A Students' Radiological Mathematics. Elementary Mathematics Applied to Medical Radiology. By L. A. W. Kemp, B.Sc., F. Inst. P., Physicist to the London Hospital; formerly Lecturer in Physics at the Polytechnic, London. Cloth. Price, $5.00. Pp. 315, with 128 figures. Blackwell Scientific Publications, Limited, 48 Broad Street, Oxford, England (Charles C Thomas, Publisher, Springfield, Illinois), 1952.

This very useful book was written by a hospital physicist for students in the fields of diagnostic and therapeutic radiology. The mathematical aspects of radiology are quite specialized and conventional mathematics texts are not designed for this field. This book is planned to satisfy and even go beyond the mathematical needs of students of radiology and is also specifically intended for those preparing for certification.

The text is divided into four sections: algebra; geometry; trigonometry; and numerical aspects of the handling of data. The first section contains four chapters and provides a workable introduction to algebra and a good discussion of the construction and significance of graphs. Good examples and problems are also given.

The second section contains two chapters which thoroughly illustrate many of the applications of geometrical principles in radiology. Some of the subjects treated are: the geometrical relationship between source, object and image, the production of magnification without distortion in parallel planes, the inverse square law, measurement of anatomical dimensions, orthoroentgenography, the localization of foreign bodies by the tube shift and no parallax methods, and methods of determining the effective size and location of a target focus spot. The treatment of these subjects is very thorough and understandable. A brief discussion of penumbra also would have been a helpful addition to this section.

The third section includes a comprehensive description of trigonometry with many examples of important applications. Logarithms and their applications, the slide rule, and nomography are treated in the fourth section. An appendix contains a very understandable introduction to differential and integral calculus. The clear presentation of the concept of the concept of the differential should be very helpful to those medical students who desire to appreciate the use of calculus. Some questions which have appeared in former D.M.R. examinations are also given in another appendix.

An important omission in this text is the mathematical application of statistical measures. Radiologists are concerned with the evaluation of reported therapeutic results, diagnostic surveys, biological experiments, etc. A description of the actual numerical application of various statistical criteria would have been appropriate and useful.

The entire text is well written and a large number of examples have been carefully chosen to demonstrate practical applications of mathematics. This book should prove very helpful to all students of radiology.

J. S. Laughlin, Ph.D.

Second Annual Report on Stress. By Hans Selye, M.D., Ph.D. (Prague), D.Sc. (McGill), F.R.S. (Canada), Professor and Director of the Institut de Médecine et de Chirurgie expérimentales, Université de Montréal, and Alexander Horava, M.D. (Lausanne), Research Associate and Librarian of the Institut de Médecine et de Chirurgie expérimentales, Université de Montréal. Cloth. Pp. 526, with numerous illustrations. Acta, Inc., 5465 Decarie Boulevard, Montreal 29, Quebec, Canada, 1952.

The Second Annual Report on Stress is a

complete compilation of something over four thousand references for the year 1952. The ever increasing literature on this subject is so voluminous that Dr. Selye has apparently enlisted the services of a research associate and librarian, Dr. Alexander Horava, to assist him in compiling the work.

As stated in the introduction, the authors say that "These volumes are published with the hope that they will act as guides to the entire literature on stress and that they will help to correlate the pertinent facts, many of which may appear to be quite unrelated."

As in the First Annual Report Selye answers the criticisms leveled against the adaptation syndrome. The authors give a brief synopsis of the stress concept as it presented itself in 1952. A definition of the terms used in connection with the adaptation syndrome and a glossary of abbreviations, symbols and special technical terms is given. In the concept of the diseases of adaptation every system of the body is affected and it is readily understandable why the yearly references reach the figure of four thousand.

Explanations as to how to use the book are given. For instance, "If several stressors, or several stimuli, affect one target simultaneously, they are registered in the position corresponding to the first of them in the list of precedence. Example [from p. 144 of this volume]: Adrenals←Cold+Fasting, in rat: If a target is simultaneously exposed to a stressor and to a stimulus, the stimulus takes precedence. Example [from p. 148]: Adrenals←Hypophysectomy +Butazolidin, in rat:"

As the authors state, due to the increasing volume of literature on stress no critical discussion of all topics is possible.

In Part III, labeled "After Thoughts," the authors outline a "Sketch for a Unified Theory of Medicine." This is naturally based upon the adaptation syndrome.

An atlas with sixteen pages of photographic illustrations representing recent observations on the effects of stress and of the adaptive hormones is found at the end of the text portion of the book.

The volume represents a tremendous amount of detailed work, and must require the services of many trained personnel, not the least of which are the secretaries and proof readers.

Certain it is that anyone interested in Selye's General Adaptation Syndrome will need this volume for reference.

Robert C. Moehlig, M.D.

BOOKS RECEIVED

Grundlagen der Röntgendiagnostik und Röntgentherapie. Von Prof. Dr. G. Schulte, Recklinghausen, und Prof. Dr. F. Kuhlmann, Essen. Dritte, neu bearbeitete Auflage. Cloth. Price, DM 29.70. Pp. 298, with 267 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1952.

Lehrbuch der Röntgendiagnostik. Von H. R. Schinz, W. E. Baensch, E. Friedl, E. Uehlinger nebst Beiträgen von E. Brandenberger, A. Brunner, U. Cocchi, N. P. G. Edling, J. Eggert, F. K. Fischer, M. Holzmann, E. Krayenbühl, Å. Lindbom, E. Lindgren, G. A. Preiss, S. Welin, A. Zuppinger. Fünfte, völlig neu bearbeitete und vermehrte Auflage. 7. Lieferung. Innere Organe. Paper. DM 89.–. Pp. 454, with 516 illustrations. Georg Thieme, Diemershaldenstrasse, 47 Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1952.

Lehrbuch der Röntgendiagnostik Von H. R. Schinz, W. E. Baensch, E. Friedl, E. Uehlinger nebst Beiträgen von E. Brandenberger, A. Brunner, U. Cocchi, N. P. G. Edling, J. Eggert, F. K. Fischer, M. Holzmann, H. Krayenbühl, Å. Lindbom, E. Lindgren, G. A. Preiss, S. Welin, A. Zuppinger. Fünfte, völlig bearbeitete und vermehrte Auflage. 8. Lieferung. Innere Organe. Paper. Price, DM 96.–. Pp. 449, with 559 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton., Inc., New York, New York), 1952.

Lehrbuch der röntgenologischen Differentialdiagnostik. Band I. Erkrankungen der Brustorgane. Von Werner Teschendorf, Köln. Dritte, verbesserte und wesentlich erweiterte Auflage. Cloth. Price, DM 129.–. Pp. 954, with 1030 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1952.

Medizinische Röntgentechnik. I. Medizinischer Teil: Skelettaufnahmen und Organuntersuchungen. Von Prof. Dr. Herbert Schoen, Karlsruhe. Cloth. Price, DM 22.50. Pp. 228, with 476 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany, 1951.

Clinical Radiology of the Ear, Nose and Throat. By Eric Samuel, M. D. (Lond.), F.R.C.S. Eng.), F.F.R. (Lond.), D.M.R.E. (Camb.), Late Hon. Radiologist the Middlesex Hospital, London; Late Radiologist Royal National Ear, Nose and Throat Hospital, London; Lieut.-Col. R.A.M.C., Advisor in Radiology to the Army; Sometime Nuffield Foundation Fellow and Duchess of Bedford Research Fellow the Middlesex Hospital, London. Cloth. Pp. 339, with 320 illustrations.

Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 49 East 33rd Street, New York 16, New York, 1952.

X-Ray Diagnosis of Chest Diseases. By Coleman B. Rabin, M.D., Assistant Clinical Professor of Medicine, College of Physicians and Surgeons, Columbia University; Associate Physician for Chest Diseases and Associate Radiologist, Mt. Sinai Hospital; Consulting Physician for Chest Diseases, Beth El Hospital; Senior Consultant for Chest Diseases, Veterans Administration. Cloth. Price, $12.00. Pp. 208, with 288 illustrations. Williams and Wilkins Company, Mt. Royal and Guilford Avenues, Baltimore, 2, Maryland, 1952.

Die zerebrale Angiographie. Von H. Krayenbühl, Professor für Neurochirurgie, Direktor der Neurochirurg, Universitätsklinik Zürich; und Hs. R. Richter, Assistent, der Neurochirurg, Universitätsklinik Zürich. Cloth. Price, D.M 59.70. Pp. 217, with 100 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New Yrok, New York), 1952.

Die Angiographie zur Erkennung, Behandlung und Begutachtung peripherer Durchblutungsstörungen. Von Dr. med. habil. H. W. Pässler, Stadtobermedizinalrat, Chefarzt des Städt. Krankenhausen Leverkusen. Paper. Price, DM 29.70. Pp. 115, with 102 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1952.

Les contusions du rein. Par L. Sabadini, Professeur de Clinique urologique à la Faculté de Médecine d'Alger, Chirurgien de l'Hôpital de Mustapha, Membre de l'Académie de Chirurgie, et J. Ducassou, Urologue des Hôpitaux (Alger). Paper. Price, 750 fr. Pp. 107, with 65 illustrations. Masson et Cie., 120, boulevard Saint-Germain, Paris 6, France, 1952.

Urethrography in the Male with a Highly Viscous, Water-soluble Contrast Medium, Umbradil-viscous U. Acta radiologica, Supplement 95. By Olallo Morales and Ragnar Romanus. Paper. Price, Sw. Kr. 20:–. Pp. 91, with 30 illustrations. Acta radiologica, Stockholm 2, Sweden, 1952.

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ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor; T. LEUCUTIA, M.D., Harper Hospital, Detroit 1, Michigan

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RADIATION THERAPY

Marquès, P., Nègre, P., Labry, A., Bru, A., and Faillières, J. Technique curiethérapique pour les tumeurs de la cavité buccale. (Curietherapeutic technique for tumors of the buccal cavity.) *J. de radiol. et d'électrol. & Arch. d'électric. méd.*, 1952, *33*, 649–651.

The authors have devised a new radium technique for the treatment of those carcinomas of the oral cavity and especially of the floor of the mouth in which interstitial application appears contraindicated. This consists in the use of a lead mold which is cast from intraoral models made individually for each case.

The procedure of taking the plaster impression of the lesion and preparing the final lead mold is described in detail and illustrated. The chamber of the mold, which contains the radium tubes, is made as wide and as high as possible to permit simultaneous employment of several tubes and treatment at a certain distance. The tubes are held in position by dental wax which is also used to create the desired distance between the radium source and the surface of the lesion to be treated. The walls of the chamber have a lead thickness of approximately 4 millimeters.

The authors evaluated experimentally the protection provided to the healthy intraoral structures by the use of such molds. They have measured with the aid of a Geiger-Müller counter (1) the percentage of absorption of the gamma rays by the lead, (2) the effect of the lead on dispersion resulting from the fact that multiple sources of radium are used, and (3) the influence of the lead on the quality of the gamma rays due to (a) absorption of the softer gamma rays and (b) addition to the primary radiation of the secondary soft radiation emitted by the lead itself.

It was found that the maximum intensity of the radiation in the region of the normal mucosa is 40 per cent of the intensity at the surface of the tumor and that there is no significant variation of the absorption coefficient. In other words, the new mold has a protective value of 60 per cent.

In clinical practice, the intraoral radium molds are used in association with external deep roentgen therapy. It is preferable to do the radium treatment first to spare the patient the pain and discomfort usually accompanying the intraoral insertion of molds in the presence of radiomucositis. Most commonly, four tubes of 5 mg. each or two tubes of 10 mg. each are placed in the chamber as widely separated as possible in a plane parallel to the surface of the lesion and dividing the chamber into two equal compartments. The mold is applied only during the day time for an average of seven to eight hours, and the total duration of the treatment with the 20 mg. source at 1 cm. distance from the lesion is 100 hours, corresponding to a dose of 15 millicuries destroyed.

Lately, the authors extended the use of this type of mold also to carcinomas involving simultaneously the floor of the mouth and the tongue and to carcinomas of the palate. They also employ the lead mold, without the source chamber, for protection of the normal structures in certain instances of interstitial radium application.

The only disadvantage of the lead mold is that it must be prepared for every patient individually. Its advantages are (1) the malleability combined with sufficient strength so that the mold can be taken out and re-inserted at will; (2) the sizable weight which permits close fitting in the mouth; and (3) the marked protective value to the normal structures.

The new technique has been satisfactorily used in 24 patients. The immediate results were good but it is too early to express an opinion on the late results. —*T. Leucutia, M.D.*

Kratzman, Emil A., and Frankel, Robert S. Roentgen therapy of peritendinitis calcarea of the shoulder; a study of 220 cases with late results. *Radiology*, Dec., 1952, *59*, 826–830.

A study is presented of 220 cases of peritendinitis calcarea of the shoulder with a follow-up report of the late results in 157 cases after roentgen therapy. The authors undertook this study in order to compare their method and results with those of others and also to determine the end-results. Only those patients who were seen three months or more after completion of roentgen therapy were considered as having had a follow-up study. The late results were obtained by personal letter and questionnaire.

Clinically the patients were classified into acute, subacute and chronic cases and the results evaluated on the basis of immediate and late responses. In general, the acute cases showed a more marked immediate improvement than the chronic cases, with the subacute cases for the most part in between, while the late results showed a similar response.

The irradiation factors for all cases were: 200 kvp.; 0.5 mm. copper with 1.0 mm. aluminum filtration; 50 cm. skin-target distance; 15 ma. Treatment was given through a 10 by 10 cm. portal over the anterolateral aspect of the shoulder, 150 r (measured in air) being administered every other day for a total dose of 450–600 r.

The authors conclude that complete relief of symptoms with return to normal motion and absolute freedom from pain is often a gradual process while the immediate responses such as pain relief and improved motion are usually remarkable and most gratifying. Their category of "over-all-aided" which refers to the combination of complete relief and improvement in the other categories showed a figure which is relatively constant in both the immediate and late results, indicating the permanency of the results.—*Donald N. Dysart, M.D.*

Bassler, Anthony. X-ray therapy in peptic

ulcer. *Rev. Gastroenterol.*, Dec., 1952, *19*, 967–972.

The author was one of the early pioneers to use roentgen therapy for the treatment of peptic ulcer and in 1910, in the first edition of his textbook (Diseases of the Stomach and Upper Alimentary Tract), he reported favorably on the results obtained. Since then he has treated a large number of cases and in this article he now again presents the "old method which, after forty years, has been rediscovered and which in my opinion has always had a special value in the medical handling of peptic ulcer when no complications exist."

Commensurate with the technical inadequacies of the time, the irradiation procedure in the beginning was based on assumptions and the dosage was quite arbitrary. A 12 inch coil unit with a "hard tube" and oiled leather filter was used. With bismuth subcarbonate in the stomach, three exposures were given in a week, usually including the entire organ. The total number of exposures varied between one and three dozen, caution being exercised not to exceed an erythema of the skin. After 1920, the technique has been gradually improved and eventually standardized.

At the present time the author proceeds as follows: A preliminary roentgenogram of the bismuth-filled stomach is made and with the aid of this the contours of the fundus and corpus of the stomach are marked on the front and back of the patient. The roentgen irradiation is carried out with 200 kv., 1 mm. Cu plus 1 mm. Al filter, 15 by 15 cm. or 10 by 10 cm. fields, and daily doses of 200 r, given alternatingly over front and back, for a total of 10 to 12 treatments depending on the thickness of the patient. It is emphasized that only the fundus and corpus of the stomach are included in the field of irradiation and not the pylorus.

The author reviews some of the salient publications of the literature on the subject, and based on these as well as his own personal observations over the many years he gives a comprehensive discussion of the underlying factors of the effect of the roentgen rays and of the various medical or surgical measures in the treatment of peptic ulcer. They all have the common purpose of reducing or depressing the gastric secretion and thereby the excessive hyperacidity. There is no doubt in the author's mind that in this respect roentgen therapy is of distinct value.

The following general conclusions are reached: (1) roentgen therapy practically doubles the medical curability of peptic ulcer and definitely saves cases from surgery; (2) the results in gastric ulcer are somewhat better than in duodenal ulcer; and (3) the presence of non-organic pyloric obstruction or frank hemorrhages is not a contraindication to roentgen therapy.

It is the author's opinion that roentgen therapy is worthy of trial in all cases of uncomplicated peptic ulcer with definite gastric hyperacidity. The irradiation may be repeated in instances of recurrence associated with re-exacerbation of the hyperacidity. —*T. Leucutia, M.D.*

BROWN, GRAYTON; SCOTT, R. KAYE; HOLMAN, W. P.; WOOD, I. J.; FINCKH, E. S.; WEIDEN, S.; and DAVIS, P. Antroduodenectomy and x-ray irradiation in the treatment of duodenal ulcer. *Lancet*, Dec. 13, 1952, *2*, 1145–1149.

The authors have been dissatisfied with the generally accepted surgical treatment of duodenal ulcer. In November, 1951, they decided to combine resection of the gastric antrum and the first part of the duodenum containing the ulcer (antroduodenectomy) with roentgen irradiation of the stomach so as to reduce the high concentration of acid and pepsin in the gastric secretion which remains after this limited resection. Antroduodenectomy was followed by an end-to-end anastomosis allowing the food still to pursue its physiological course.

Three plans for the treatment of chronic duodenal ulcer were tried: roentgen irradiation alone; antroduodenectomy followed two months later by roentgen irradiation; and roentgen irradiation followed two months later by antroduodenectomy.

The patients in each group were studied by the following methods:

Clinical observation, special attention being paid to appetite, abdominal discomfort, weight, and general sense of well-being.

Serial histamine test meals using 0.3 mg. of histamine immediately before and two weeks after operation, immediately before and after irradiation, then usually at monthly intervals for six months, three-monthly till the end of a year, and finally six-monthly.

Serial "overnight" test meals at intervals of three to six months; also occasional insulin test meals.

Serial gastric biopsies before and two months after operation, before and after irradiation, then at intervals of one or two months for six months, and then at longer intervals.

Ten patients with chronic relapsing duodenal ulcer were subjected to roentgen irradiation only. This consisted of the administration of 2,000 r during three weeks centering over the stomach. Serial tests meals and gastric biopsies showed a moderate radiation effect lasting from six to nine months. With return of the secretion, and the biopsy findings, to their original state, 4 of the 10 patients had a severe relapse of their ulcer symptoms.

Treatment by antroduodenectomy followed two months later by roentgen irradiation was carried out in 10 patients. These patients have been followed from one to eight months and have enjoyed excellent health free from dyspepsia, taking full unrestricted diet and no antacids or other medical treatment.

The ideal plan appeared to be first to reduce the acid secretion by irradiation and then perform antro-

duodenectomy two months later. Two patients were subjected to this procedure. Both patients pursued a highly satisfactory course and are now well four and seven months after operation.

The authors conclude that the treatment of chronic duodenal ulcer by antroduodenectomy and roentgen irradiation is encouraging; however, many years must pass before a significant comparison with other methods can be made.—*William C. MacCarty, Jr., M.D.*

Pack, George T., Gerber, David M., and Scharnagel, Isabel M. End results in the treatment of malignant melanoma; a report of 1190 cases. *Ann. Surg.*, Dec., 1952, *136*, 905–911.

This report is based on 1,190 cases seen from 1917 to 1950, representing the largest series of malignant melanoma ever analyzed. The cases are divided into determinate and undeterminate groups. The undeterminate group includes those patients who could not be located for a five year follow-up after treatment, those who refused treatment, and those dying from other causes. Of the 744 determinate cases, 575 were used in the study, as the end results in the patients treated from 1946 to 1950 are not as yet known. One hundred and twenty-three patients of the 575 were free from melanoma at the end of five years, giving a 21.4 per cent five year survival rate. In malignant melanoma, probably more than in any other malignant tumor, a five year postoperative survival without recurrence is a valid criterion for a cure.

In the authors' series, malignant melanoma occurred more frequently on the head and neck (22.1 per cent) excluding the eye and oronasal mucosa, and on the sole of the foot (9 per cent). The high incidence of head and neck involvement was believed to be due to the large number of patients with tumors of the head and neck seen at the Memorial Cancer Center and not to the true incidence of the melanoma in this location. The involvement of the sole of the foot was thought to be a reflection of its true incidence.

Low five year survival rates were found in oronasal lesions (91. per cent), anal-rectal lesions (0 per cent) and trunk lesions (13.7 per cent). Higher survival rates were obtained in the subungal lesions (38.9 per cent) and palm lesions (87.5 per cent), although there were too few palm cases to be of statistical significance. The low survival rates in the head and neck lesions were due, probably, to less radical surgery in these areas. The extensive lymphatic drainage accounted for the low survival rate in the trunk lesions.

The authors doubt that there is a real sex difference in the five year survival, although it was 15.6 per cent for the males and 27.4 per cent for the females. Women are more cancer conscious and therefore usually report earlier for treatment.

There was no difference in the prognosis depending on age after puberty. Prepubertal melanomas were not included in this study.

The prognosis was only one-half as good in those cases in which definite surgery was delayed over one month after local excision. The authors state that surgical treatment offers the best chance for a cure and that radium and external irradiation are no longer used at the Memorial Cancer Center as a primary form of therapy. Surgical procedures are classified into four types: (1) wide local excision; (2) wide local excision and radical dissection of adjacent lymph nodes; (3) wide local excision in continuity with radical dissection of adjacent lymph nodes; and (4) radical amputation of an extremity. There were 40.5 per cent five year survivals when the last three procedures were used and no metastases were present. If metastases were found, the five year survival was 14.1 per cent.

The authors conclude that adequate surgical treatment should be instituted promptly in cases of melanoma and that the best chance for a cure is at the time of the first excision.—*Charles W. Cooley, M.D.*

Leadbetter, W. F. Treatment of testis tumors based on their pathological behavior. *J.A.M.A.*, Jan. 24, 1953, *151*, 275–280.

Prompt exploration of a suspicious lesion of the testis is recommended. Orchiectomy is carried out if a tumor is found, through an inguinal incision performed so that the cord is ligated above the internal inguinal ring.

Patients with pure seminoma without demonstrable metastases should receive deep roentgen therapy to the entire retroperitoneal area in amounts of 2,000 r per port tissue dose. If obvious metastases are present above the diaphragm these should be treated concomitantly.

Embryonal carcinomas and teratocarcinomas without supraclavicular, mediastinal, pulmonary or extensive retroperitoneal metastases should probably be treated by unilateral retroperitoneal lymph node dissection. If more than a few positive lymph nodes are present, subsequent contralateral retroperitoneal lymph node dissection is probably desirable.

Chorionepitheliomas have such a completely poor prognosis that therapy other than orchiectomy seems valueless.—*James J. McCort, M.D.*

Reichenmiller, H., and Drescher, H. Ein einfaches Radiuminstrumentarium für gynäkologische Zwecke. (A simple armamentarium for radium therapy in gynecology.) *Strahlentherapie*, 1952, *89*, 61–71.

The authors for many years have utilized radium in gynecologic therapy on the principle that each patient's treatment must be individualized. Certain instruments for inserting and handling radium and certain types of containers to serve as radium applicators have become standard with them, however.

This armamentarium is described in considerable detail.—*Henry G. Moehring, M.D.*

PORTMANN, U. V., and MCCULLAGH, E. PERRY. Developmental defects following irradiation of the ovaries in a child. *J.A.M.A.*, Feb. 28, 1953, *151*, 736–737.

The case reported is that of a female child who developed a slowly enlarging tumor at the age of fifteen months. The tumor was located in the pelvic cavity and was firmly attached to the bifurcation of the aorta and could, therefore, not be removed. Microscopically, the tumor was apparently a neuroblastoma. The authors gave the patient two courses of deep roentgen therapy, the total dose from both courses being about 1,300 roentgens. This amount of irradiation was sufficient to melt the tumor so that it could no longer be felt.

The patient has been examined periodically for eighteen years since the treatment was given. At the age of seventeen, she had not menstruated; the bone age at that time, showed a degree of skeletal maturity of about 13½ years. 'There was a much greater degree of interference with the development of the bones of the pelvis than elsewhere in the body. Urinary gonadotrophin levels were markedly elevated and this is considered consistent with primary ovarian failure resulting in pituitary hyperactivity.

Interesting physical developments were obtained by the use of estrogen therapy in overcoming the effects of the ovarian deficiency.—*R. E. Kinzer, M.D.*

BIVENS, MELVIN D. Primary carcinoma of the vagina; report of forty-six cases. *Am. J. Obst & Gynec.*, Feb., 1953, *65*, 390–399.

The author reports on a series of 46 cases of carcinoma of the vagina seen between 1930 and 1950. It is a rare disease. Williams of the Boston City Hospital is quoted as reporting only 2 cases from 1906 to 1930.

The average age was sixty-four years, the youngest patient being twenty-four and the oldest eighty-three years of age.

Prolonged use of a pessary and senile vaginitis seemed to be the two most important predisposing causes.

Painless abnormal bleeding, leukorrhea, a tumor mass and pain were the most common symptoms in this order of importance. Sixty-seven per cent of the patients had bleeding and 8 per cent had leukorrhea.

Forty-eight per cent of the lesions were located in the upper third of the vagina and 21 per cent involved the posterior wall.

Clinically, the lesions were classified as spongy, friable and highly vascular (28 per cent); infiltrating or circumscribed (54 per cent); and annular (6.5 per cent). This description is based on Healy's staging.

Ninety-five per cent of the patients had extravaginal extension of their disease when first seen. This means extension into the parametria, bladder, rectum or bone. Four cases had skeletal metastases and 1 had pulmonary metastases.

Forty-three cases had squamous cell carcinoma, and of this group, 52.7 per cent were Grade 3 lesions. Three cases had papilliferous adenocarcinoma.

The absolute five year survival rate was 27.5 per cent. Four patients were treated with radium alone, 6 with roentgen therapy alone, 28 with radium and roentgen therapy, and 8 with a combination of surgery and roentgen therapy or radium.

Coutrial reported 45.4 per cent of 22 patients alive and well at five years after radium and roentgen therapy. His figures and staging are used as a comparison basis. Of 4 patients in Stage I (by following Coutrial's staging) there were 4, or 100 per cent, surviving at five years; of 23 patients in Stage II, there were 7, or 30 per cent, surviving five years; and of 13 patients in Stage III, there were none surviving at five years. These are the author's figures with the staging broken down according to Coutrial's clinical classification.

It is suggested that if carcinoma of the lower third of the vagina is treated as carcinoma of the vulva and carcinoma of the upper third of the vagina is treated as carcinoma of the cervix the survival rates might be expected to be higher.—*F. W. O'Brien, Jr. M.D.*

FLETCHER, GILBERT H. Cervical radium applicators with screening in the direction of bladder and rectum. *Radiology*, Jan., 1953, *60*, 77–84.

The author discusses the applicators which combine the uterine tandem and the colpostat in one rigid piece and mentions several disadvantages found in their use. A somewhat different applicator developed along the Manchester line using ovoids of 2.0, 2.5, and 3.0 cm. in diameter and of slightly different lengths is described.

These ovoids are not oval in shape because one dose not want an isodose surface and, in order to reduce the dosage in the direction of the bladder and rectum, tungsten buttons are inserted at each end for the purpose of screening. The tungsten buttons are not of uniform shape; the rectal side button being a half disk and the bladder side button a 150° sector. They are located to provide maximum screening for the anterior rectal wall and trigone of the bladder without decreasing the radiation in the direction of the uterosacral and broad ligaments. Each cylinder is fastened to a separate handle which are easily-locked together, the ovoids having a range of separation from contact to 4 cm. This arrangement allows for greater adaptability to fit the different sizes and shapes of the vault and fornix.

The loading of radium depends on the separation of the ovoids with 15–20, 20–25, and 25–30 mg. being used respectively in small, medium and large cylinders. The uterine tandems, depending upon their length, are loaded with 15, 15–10, 15–10–10 mg. The application time is determined by the measurements

in bladder and rectum, not to exceed 3,500 gamma roentgens to the bladder and 3,000 gamma roentgens to the rectum at each application. A second application is made ten days later. If colpostat and uterine tandems are used separately the insertions are made weekly (three or four). Radium therapy usually precedes external irradiation except in larger or infected or markedly ulcerating lesions with obliteration of one or two fornices.—*Donald N. Dysart, M.D.*

Gárciga, Carlos E. Conceptos sobre la radioterapia en el cáncer del cuello del útero. (Concepts on radiotherapy of carcinoma of the uterine cervix.) *Arch. cubanos cancerol.*, Jan.–June, 1952, *11*, 46–54.

The principles guiding radiation therapy of cancer of the uterine cervix in the Radiotherapy Department of the Radium Institute are outlined. These are based on the experiences of the past eleven years.

A League of Nations classification of carcinoma of the cervix is made at the beginning of treatment. The irradiation is protracted over a period of from six to eight weeks. In general, two anterior, two posterior, two inguino-iliac and two sacroiliac portals are used where the anatomical configuration of the patient permits. Angulators control the direction of the roentgen beam.

External roentgen therapy is considered to be the most important part in the treatment of carcinoma of the cervix, although either radium or transvaginal roentgen therapy is also used.

The advantages of transvaginal roentgen therapy are: (1) more homogeneous irradiation of the cervix and fornices; (2) wider margin of safety between tumor destruction and protection of normal tissues; (3) in tumors of cervical stump, it is the treatment of choice; (4) it permits accurate calculation of daily dose; (5) in crowded departments more patients can be treated by this technique; and (6) it is less likely to produce thickening of the vaginal wall as compared with radium treatment. The disadvantages include: (1) necrosis of the vulva because of insufficient protection; (2) radioepithelitis or necrosis of the bladder and rectum ; and (3) intestinal complications.

Transvaginal roentgen therapy can be carried out with medium voltage equipment. The principal cause of failure is insufficient dosage to the tumor and the tumor bed as a result of incorrect positioning, inadequate voltage and location of portals, particularly in obese patients.

Failures in radium treatment may be due to inadequate dosage, improper application or displacement of the radium after insertion.

These technical failures are more frequently responsible for poor results than the so-called low curability of the tumor.—*Murray M. Friedman, M.D.*

Percival, Eleanor. A twenty-year study of radiological treatment of cancer of the cervix at the Montreal General and Royal Victoria Hospitals. *Am. J. Obst. & Gynec.*, Feb., 1953, *65*, 386–389.

The author reports on 1,200 cases of cancer of the cervix treated between 1927 and 1946 at the Royal Victoria and Montreal General Hospitals. These were classified clinically as follows: Stage I, 137 cases; Stage II, 264 cases; Stage III, 553 cases; and Stage IV, 246 cases.

The Stage I, II, and III lesions were treated with radium followed by external irradiation.

The radium was given in two seances. Two 25 mg. sources in tandem were placed in the cervical canal and three 25 mg. sources were placed in the vagina and vaults; these were left in position for twenty hours (2,500 mg. hr.). The second treatment was repeated in ten days for a longer period. The importance of thorough vaginal packing is emphasized.

External irradiation was carried out with 200 kv., corresponding to a half-value layer of 0.9 mm. copper, through two anterior and two posterior 10×15 cm. fields, sparing the midline. A tumor dose of between 1,800 and 2,300 r was delivered. External irradiation was occasionally used initially where there was too great a pelvic inflammation and was used almost exclusively in the Stage IV lesions.

At the end of five years, 72 per cent of the patients with Stage I lesions, 56 per cent of the patients with Stage II lesions, 30 per cent of the patients with Stage III lesions and 7 per cent of the patients with Stage IV lesions were alive and well.

Dividing the series into two decades, it is noted that those patients treated in the latter ten year period had a greater percentage survival. This is partly due to a greater percentage of early cases.

The importance of supportive measures such as antibiotics and vitamins is stressed.

Complications as usually seen did occur. Their incidence was considerably lower in the second ten-year period. Twenty-three per cent of 72 patients treated prior to 1939 experienced side reactions, whereas only 6.5 per cent of 216 patients treated after 1939 developed complications.

The problem of treating radioresistant cancer of the cervix is briefly discussed. As the author states, it would, of course, be desirable to know in advance which cases were going to be radioresistant.—*F. W. O'Brien, Jr., M.D.*

Montgomery, John B., Long, Joseph P., and Hoffman, Jacob. A clinical evaluation of the use of radium therapy in the control of benign uterine bleeding. *Am. J. Obst. & Gynec.*, Nov., 1952, *64*, 1011–1020.

For many years the use of radium to control benign uterine bleeding has been unchallenged, but occasionally the question is raised whether its use

promotes the incidence of uterine malignancy. This prompted the authors to review the patients treated by the Division of Gynecology, Jefferson Medical College and Hospital.

The technique involved the insertion of radium following curettage and biopsy of the cervix when indicated. Two capsules of 50 mg. of radium were used, in some patients with 0.5 mm. Pt equivalent, in others with 1.5 mm. Pt filtration; more recently, multiple 5 mg. capsules with 0.5 mm. Pt filter were substituted. The dosage varied from 300 to over 2,500 mg. hr., most frequently being between 600 and 1,500 mg. hr.

The material consisted of 851 treated cases of benign uterine bleeding followed for six months or more. They were divided into dysfunctional bleeding and bleeding with myomas. The patients were thirty-five years old or older and the uterine scrapings showed varying degrees of activitiy.

Satisfactory results were obtained in 93.1 per cent of the dysfunctional group, most of the unsatisfactory results being in the younger women who received smaller doses. Of the 36 failures in this group, 19 were re-irradiated and in 16 the result was satisfactory. Six of the 36 failures were placed in this category because of the subsequent development of cancer, 5 in the corpus uteri and 1 in the ovary.

In the myoma group satisfactory results occurred in 87.4 per cent. Most of the failures were in younger women (who received smaller doses) and in women whose uteri were larger than that of twelve weeks gestation. Of the 41 failures, 19 were re-irradiated and a satisfactory result obtained in 13. In these 41 failures malignancy developed in 6 cases, 4 in the corpus and 2 in the cervix.

Thus pelvic malignancy after irradiation occurred 12 times in the entire series, an incidence of 1.4 per cent. The cases were rather evenly distributed between four and eighteen years after treatment, except for 1 case found after hysterectomy one year after treatment which was probably missed on the original curettage. The radium dosage received by these cancer patients varied between 300 and 1,800 mg. hr.

The authors conclude that there is no evidence in this series to indicate increased incidence of malignancy following radium treatment of benign uterine bleeding. The good results justify continued use of the method, and proper selection of cases with adequate dosage (probably 1,500 mg. hr.) will improve the results.—*Henry J. Klos, M.D.*

O'BRIEN, FREDERICK W., JR. Some aspects of supervoltage roentgen therapy. *Am. J. Surg.*, Jan., 1953, *85*, 62–66.

The author gives an excellent review of the development and present status of supervoltage roentgen therapy by referring extensively to the various sources available in the literature.

Of the many factors contributing to the proper approach to this form of therapy, he pays special attention to the following: (1) clinical and microscopical evaluation of the tumor; (2) sensitivity of the tumor to radiation; (3) quality of radiation; (4) treatment time; (5) field size; (6) depth and size of lesion; (7) number of portals used; (8) distance and filtration; (9) patient's general condition, and (10) reponse of lesion during and after treatment.

The main advantages of supervoltage roentgen therapy over conventional 200 kv. therapy are: (a) increased skin tolerance due mainly to the high energy photons which produce long range secondary electrons in the tissues resulting in lesser ionization near the surface; (b) increased percentage depth dose which is the result of greater penetration of the harder rays, and (c) greatly decreased tangential and circumferential scattering with marked increase in the forward scattering which improves the useful beam.

The author sounds a word of caution in treating with supervoltage roentgen rays. Since the skin is no longer a limiting factor, the deep tissue reactions, especially of the mucous membranes, must be carefully noted and in case of crossfiring through several portals the magnitude of the exit dose must be taken into consideration. Scrupulous observation of protection factors is also important.

Rotation therapy with supervoltage roentgen rays allows a concentration of the dose at the tumor site with further reduction in the damage to the skin and intervening tissues. Therefore, it is well suited for the treatment of deep-seated midline lesions, as, for example, of the esophagus, mediastinum, pituitary gland, nasopharynx, hypopharynx, bladder and perhaps of the uterine cervix. Since a misdirected concentration of the beam may lead to very severe damage of the surrounding normal structures, unpresaged trouble may occur whenever the exacting technical requirements of this type of treatment are not fully met.

In concluding, the author states that by using supervoltage roentgen therapy the ability to deliver to deep-seated tumors a greater dose with less damage to the skin undoubtedly offers a chance of a cure to a selected group of cancer patients. It is anticipated that in the near future reports on a statistically significant number of curable cases will be published.

A bibliography of 33 articles is appended.—*T. Leucutia, M.D.*

POHL, R. Funktionssteigerung der Nebennierenrinde durch Röntgen-Kleindosen. (Increase in the function of the suprarenal cortex with small doses of roentgen rays.) *Wien. klin. Wchnschr.*, March 13, 1953, *65*, 211–214.

The author attempted to increase the secretion of steroids by irradiation of the suprarenal cortex with small doses of roentgen rays.

Three cases with a septic course (1 case of poly-

arthritis, 1 of cholangitis and 1 of thrombophlebitis) are reported in detail in which daily roentgen ray doses of 20 to 30 r achieved definite improvement and rapid cure.

The effect of irradiation paralleled that of cortisone administration: drop of temperature, euphoria, decrease of pain and swelling and increase of appetite. The sedimentation rate remained high for a long time while the patients were symptom free. The best response was obtained in apathetic patients.

A functioning suprarenal cortex is, of course, necessary for a response. A test to aid in the selection of patients best suited for this type of treatment is being sought and more patients will have to be treated before this method of therapy can be accepted.—*Frederick M. Reis, M.D.*

Baden, Kurt. Erfahrungen mit fractionierter Röntgenepilation. (Experiences with fractionated roentgen epilation.) *Strahlentherapie*, 1953, *90*, 494–498.

Fractionated irradiation for epilation eliminates, or greatly decreases, the disadvantages of single dose epilation. The tolerance dose is increased though the dose required for epilation is increased but little by fractionation. Undesirable side-effects are avoided. The epilation dose may be repeated after three months without hazard.

For epilation of the scalp, 150–200 r (measured in air, with 1.0 mm. Al filter, half-value layer of 0.025–0.05 mm. copper [An accompanying figure equates this with 60–80 kv.] and 70–100 r/min.) are administered to each of five 100–175 sq. cm. fields at intervals of 2–4 days for a total of three such doses to each field. If the fields are severely inflamed, the dosage can be fractionated even more.—*Henry G. Moehring, M.D.*

DeCoursey, Elbert. Effects of midlethal doses of total body ionizing radiations. *J.A.M.A.*, March 14, 1953, *151*, 904–905.

The effects of ionizing radiations on tissues, whether from alpha, beta, proton or neutron particles or from gamma or roentgen rays, are qualitatively the same, and may be easily classified as cellular, intercellular and vascular. Not only the total amount but the rate of absorption is important. The author lists tissues in their order of radiosensitivity, which is in agreement with other publications. In total body irradiation consideration of the relative importance of each tissue in the order of decreasing radiosensitivity is paramount.

Hemopoietic elements. These are the most radiosensitive in the body. In the Japanese casualties there was rapid depletion of bone marrow and lymphoid cells throughout the body. This led often as early as the second day to a striking leukopenia and a slower but progressive oligocythemia, with the result that infection was noted in the third to sixth week, a hemorrhagic syndrome in the fourth week and profound anemia in the second and third months. Active restoration of all hemopoietic cells to normal numbers at the end of three months was the rule in Japanese survivors.

Intestinal mucosa. Epithelial cells in the crypts of ileal glands are next in sensitivity. They showed radiation injury during the first two weeks evidenced by a few small ulcers.

Reproductive organs. Radiation injury was temporary and had little influence on the survival of individual patients.

Skin. The main effects were ulceration, epilation, and in the eye lenticular opacities.

Endothelium. Vascular permeability was observed either as a direct radiation effect on the endothelium of blood vessels or secondary to thrombocytopenia.

Other tissues. Changes were largely indistinct.

It follows from the aforementioned that a clinically important mid-lethal dose, that is a total body dose which is fatal to 50 per cent of those exposed, is manifested mainly by aplastic anemia and gastrointestinal injury.—*Wallace M. Roy, M.D.*

Mondry, Felix, and Montag, Caspar. Beitrag zur Behandlung des Phantomschmerzes. (A contribution to the management of phantom pain.) *Strahlentherapie*, 1953, *90*, 19–24.

Twenty-three amputees with severe phantom pain, many subjected to previous fruitless therapy, were treated by a combination of surgical means and roentgen therapy. Eighteen were so much benefited that they could be classed as cured. Two patients were considerably improved. Only 3, in whom extenuating circumstances existed, had unsatisfactory results.

The management of these patients was based on the premise that latent or smoldering infection plus extensive scarring in the stump was at the root of the phantom pain.

The stump was surgically corrected. Then to ensure undisturbed healing, high doses of penicillin were administered for two weeks. When the wound was healed, in five to twelve days, roentgen therapy was begun. The first dose was 100 r (180 kv., 1 mm. Cu h.v.l., 100 r/min.) to a 20×24 cm. field. This yielded a depth dose of approximately 50 r to a femoral stump. Two days later a similar dose was administered. Then the dose was increased to 200–300 r every two or three days to a total depth dose at the center of the stump of 1,300–1,400 r in two to three weeks.

On the same day as the third roentgen treatment of the stump, treatment of the proper (lumbar or cervical) sympathetic nerve trunk and neighboring spinal cord was begun; 200 r repeated 5–6 times to a 10×15 cm. field yielded a depth dose of approximately 700 r.—*Henry G. Moehring, M.D.*

PAPE, R. Röntgentherapie des Schmerzes. (Roentgen therapy of pain.) *Wien. klin. Wchnschr.*, Jan. 23, 1953, *65*, 81–84.

The author discusses the mechanism and effect of roentgen therapy on pain in the following conditions:

1. *Wounds and Inflammations.* The main causative agents of the pain are edema, retained secretions, hyperemia, cellular infiltration and nerve irritation. Most radiologists believe that the clearing of exudate is the reason for pain relief. Glauner showed that such is not always the case and that the disappearance of the pain may be due to the effect on the nerve endings in the capillary walls.

Joint effusions, post-tooth extraction pain, sinusitis (5–10 r relieves pain), otitis, mastoiditis, chronic and subacute osteomyelitis, furuncles, mastitis, etc., all benefit from roentgen therapy. In degenerative joint diseases, the author has used 1 to 20 r, in 500 cases, with good palliation in most. In acute inflammatory effusions of the joint, irradiation of the mid-brain, and also of the adrenals has been done with good effect in some cases.

2. *Neuralgias.* Sciatica and trigeminal neuralgia may be relieved by doses smaller than 50 r. Relief of pain is due probably to destruction of the inflammatory cells. However, since such relief may be obtained with doses considered too small for such an action, the author believes that the effect is on the nerves. He gives 2 to 3 treatments per week for a maximum of 8 treatments, with each dose very seldom exceeding 20 r.

3. *Vascular Pains.* The author uses 5–10 r on the adrenals and vertebral segments in intermittent claudication. In migraine, the mid-brain and adrenal glands are irradiated.

4. *Tumors and Granulomas.* Pain relief is due to the effect on the vascular and nerve structures at first. The author gives 5 to 10 r by total body irradiation in far advanced carcinomatosis to get an effect from the vegetative system.—*Samuel Richman, M.D.*

KIRCHHOFF, HEINZ, and IMHOLZ, GERT. Spontanfrakturen des Schenkelhalses nach Röntgenbestrahlung wegen Genitalcarcinom. (Spontaneous fractures of the femoral neck after roentgen irradiation of genital carcinoma.) *Strahlentherapie*, 1953, *90*, 199–207.

Of 1,500 women treated for genital carcinoma from 1944 to 1951, 14 developed fractures of the femoral neck; 2 of them had bilateral femoral neck fractures. Two of the fractures were so tenuously connected with the radiation therapy that they are practically dismissed. The majority of cases received "Coutard-Kirchhoff" roentgen irradiation for carcinoma of the cervix. This consisted of 6–8 treatments of 400 r each (180 kv., 6 ma., 40 cm. f.s.d., 1 mm. Cu filter) to 10×15 cm., right and left, anterior, posterior and lateral fields.

Almost all of the 12 cases counted as due to irradiation showed additional damage to the regional vascular system; *i.e.*, induration, telangiectasis, hematuria, or bleeding from the bowel.

These evidences are listed as proofs that a given fracture is the result of irradiation: (1) The average age of the patients was considerably below the average age for "senile" fractures. (2) Regional vascular damage resulted from the irradiation. (3) All other causes of fracture were ruled out, both by histologic examination of tissue obtained at open reduction of the fracture and by the subsequent clinical and roentgenographic observations. (4) Irradiation was administered through lateral ports, though undoubted post-irradiation fractures are known in patients who received no radiation through lateral ports. (5) A positive time-relationship existed between irradiation and the occurrence of the fracture, amounting to 3–24 months in most of these cases.

Clinical experience taught that a woman who complains of swelling of the thigh, rheumatic pains, or disturbance of gait after radiation therapy should be examined specifically for fracture of the femoral neck.

Clinical condition of the patient permitting, operative treatment of the fracture yielded the best functional results and the shortest period of disability.—*Henry G. Moehring, M.D.*

TUDWAY, R. C. The place of external irradiation in the treatment of osteogenic sarcoma. *J. Bone & Joint Surg.*, Feb., 1953, *35-B*, 9–21.

The author believes that external irradiation has a definite place in the curative treatment of certain cases of osteogenic sarcoma. There is no simple formula which indicates how these tumors should be dealt with. He states the decision must rest on the assessment of several factors. It is especially important that a positive diagnosis be made, otherwise there is no firm ground on which to determine the treatment. In this article, a total of 33 cases are considered, 8 representing osteolytic and 25 osteoblastic osteogenic sarcomas. No attempt is made to derive statistical deductions, since the number of cases is too small. Eight patients survived for two years or more after treatment—all from the osteoblastic group; 4 of these survived for five years or more. There were no survivors from osteolytic tumors.

The subdivision of cases into osteoblastic and osteolytic types was useful in assessing the prognosis. The distinction was based on the roentgenographic appearances. Histopathologically, about half of the osteolytic tumors in the series were of the spindle cell variety, but only 1 of the osteoblastic type was spindle celled, the rest being polyhedral celled. There was a high proportion of histopathological Grade 3 tumors among the osteolytic cases.

Treatment had little influence on the course of the osteolytic tumors. This was perhaps largely due to the fact that most of the tumors occurred in the axial skeleton were neither amputation nor effective irradiation was possible. Except for 1 case in which the patient died soon after admission to the hospital, palliative deep roentgen therapy was given in all cases. A dosage of over 5,000 r produced good symptomatic relief in some, but in no cases of osteolytic tumor was there evidence of real arrest of the tumor growth. Osteolytic sarcomas commonly arise in previously abnormal bone and in older patients. These two factors usually go together and, as in the case of osteoblastic tumors, are associated with poor prognosis.

As far as the roentgenographic appearances were concerned, there was no clear-cut criterion by which the cases could be classified. On the whole, the group with better prognosis showed a predominance of bone reaction over destruction, and the cortex was expanded or thickened rather than destroyed. Subperiosteal new bone formation was present, perhaps markedly so, but evidence of erosion of this new bone was absent or slight, and was late in appearance, Sunray spicules were not marked. Codman's "triangle" was absent in these cases and this was perhaps the only clear sign. This led to the opinion that in the group of atypical cases of better prognosis, where a distinction between an inflammatory lesion, on the one hand, and a malignant tumor, on the other, was most needed, those reoentgenographic features that tend to define the case as malignant were absent.

Osteolytic sarcomas tend to arise centrally, showing a central area of destruction which involves the cortex without expanding it, and produces some periosteal reaction. Fever was not a noticeable feature in the cases of the author's series. The study of the series would seem to indicate that there is a group of osteogenic sarcomas in which the prognosis is better than average. It is not, however, a clear-cut group. It may be indicated by an atypical history, in which at first symptoms and appearances favor an inflammatory lesion of bone. Or it may be indicated by an indefinite roentgenographic picture, which again resembles that of an inflammatory condition or other benign change within the bone. This group of atypical osteogenic sarcomas may possibly turn out to be separable from the others as a distinct variety, just as primary reticulosarcmoa of bone has been separated from Ewing's tumor. There is, however, no pathological evidence of such a distinction so far.

A more definite indication of this relatively favorable group is given by pathological grading after biopsy. A fairly reliable and precise grading, according to Tudway, is given by the mitotic ratio. He emphasizes that in most cases of his series in which treatment was given by irradiation alone, the dosage was suitable for growth restraint rather than attempted cure, and was often given in repeated courses.

The author's summary is as follows:

1. Deep roentgen therapy in high dosage, followed by local resection should be given serious trial especially: (a) in the upper limb; (b) in the group with atypical clinical and roentgenographic signs, or histopathology resembling that of inflammatory lesions; (c) with Grade 1 histopathology; and (d) in the young.

2. Deep roentgen therapy followed at once by amputation should be used for osteogenic sarcoma: (a) if local resection would leave a lower limb more unstable than an artificial leg; or (b) if response to roentgen therapy is poor.

3. Deep roentgen therapy alone should be used: (a) if the patient is unsuitable for, or refuses, any operation; and (b) palliatively, if metastases are present or the tumor is too far advanced, or the patient is not fit for radical treatment.

4. Amputation alone should be used palliatively, for pain or fungation, when roentgen therapy has failed to relieve, or is not readily obtainable.

5. Biopsy and histopathological grading must be performed in every case. A histopathological diagnosis is most important.

6. The records of every possible case should be sent to and discussed by a group with special experience of these tumors.

The author also states that it is, of course, recognized that supervoltage roentgen therapy, the assistance of biochemical factors, or even a rearrangement of time-dosage relations may alter the picture of the treatment at any time.—*Ralph S. Bromer, M.D.*

RADIOISOTOPES

MacIntyre, William J., Storaasli, John P., Krieger, Harvey, Pritchard, Walter, and Friedell, Hymer L. I^{131}-labeled serum albumin: its use in the study of cardiac output and peripheral vascular flow. *Radiology*, Dec., 1952, *59*, 849–857.

A study concerning cardiac output and peripheral vascular flow is made using serum albumin labeled with I^{131}. For determination of the cardiac output, the labeled albumin is injected into the antecubital vein as rapidly as possible, and the radioactivity of the blood in the femoral artery is determined; and from this, the cardiac output is calculated by use of the dilution principle. Momentary count rates are difficult to obtain accurately with tracer doses and the authors accomplished this by the use of a 3 mm. cannula placed in the femoral artery which directs a continuous sample of blood in close proximity to a sensitive scintillation counter. The output of the scaler is directed to a two-channel counting rate computer which eliminates the "memory" effects of such computers and the results were recorded by an Esterline-Angus graphic meter. From these data, the aver-

age concentration of I^{131} in the first circulatory cycle is determined, thereby allowing calculation of the cardiac output. Experimental results on 8 dogs show this method to give an average of 9 per cent higher readings when compared to the cardiac output as determined by means of a rotameter.

Also, the above recording apparatus used in conjunction with iodinated albumin may be used to study peripheral vascular flow. The activity of the soft tissues with respect to time is measured over the sole of the foot and from these data, equilibrium curves are plotted. The rate at which equilibrium is reached is, in general, a function of the peripheral flow. The level of activity reached at equilibrium is a function of the amount of blood present. Hence, when arterial obstruction is present, the activity rises slowly to a low equilibrium level, while in venous obstruction the activity rises at a normal rate but maintains equilibrium at a higher than normal level.—*Martin B. Goodwin, M.D.*

HORST, WOLFGANG, and RÖSLER, HELMUTH. Der Transport des Hormonjods im menschlichen Serum intersucht mit Papierelektrophorese und Radiojod. (Zugleich ein Beitrag zur Frage der Existenz von sog. Zwischenfraktionen.) (A study of the transportation of hormonal iodine in human serum with paper electrophoresis and radioiodine; also a contribution to the question of the existence of so-called intermediary fractions.) *Klin. Wchnschr.*, Jan. 1, 1953, *31*, 13–17.

The authors studied the position of hormonal iodine in the serum-protein spectrum, using radioiodide (I^{131}) and paper electrophoresis. Observations were made on 12 patients with hyperthyroidism, who had been given doses of between 3 and 30 millicuries of I^{131}, on 3 patients with carcinoma of the thyroid, who had been given 100 millicuries of I^{131} and on 5 rats, who had been given 1 to 2 millicuries subcutaneously. The amount of total I^{131} in per cent of the applied dose per liter serum, the protein-bound part of I^{131} (after precipitation with trichloroacetic acid) and that part of the protein-bound iodine which could be extracted with butanol were determined in all patients.

In 82 single electrophoretic studies it was found that the largest amount (about 85 per cent) of organic serum iodine is found in a fraction moving between the α_1- and α_2 globulins, called "inter-α-fraction" and the smaller part (about 15 per cent) in the albumin fraction. It was not possible to demonstrate the existence of this inter-α-fraction by amido-black dye, probably because its concentration is too low, but its existence can be proven indirectly. No satisfactory explanation has as yet been advanced for the fact that in normals and in hyperthyroid cases about 85 per cent of the hormonal iodine obtained by butanol extraction is being transported by the inter-α-fraction and about 15 per cent by the albumin fraction. One may assume that the butanol extract is a chemically uniform substance which is distributed in the ratio 85:15 in the fraction. On the other hand, it is also possible that there are two chemically different iodine-containing substances of the extract, one of which is transported by the inter-α-fraction and the other by the albumin fraction. Analysis of iodine metabolism in the cases of carcinoma of the thyroid with metastasis has opened up some new aspects although the number of cases is too small to come to any definite conclusions. In one of these cases the ratio of the two fractions was 58:42 on the first day and changed to 38:62 in a few days. This is contrary to the findings on hyperthyroid patients where the ratio on the same patient does not change with time.

Further studies may bring more light into the questions of indications for iodine therapy in malignancies of the thyroid and in the prognosis of this type of therapy.—*Otto Glasser, Ph.D.*

CLARK, D. E., RULE, J. H., TRIPPEL, O. H., and COFRIN, D. A. Five year experience with radioactive iodine in treatment of hyperthyroidism. *J.A.M.A.*, Nov. 29, 1952, *150*, 1269–1272.

The 384 patients in this series were followed from six months to sixty months.

One or more of the following criteria for the selection of patients for I^{131} therapy were met: (1) uncomplicated hyperthyroidism in patients over forty years of age; (2) recurrent or persistent hyperthyroidism after thyroidectomy; (3) hyperthyroidism with severe cardiovascular disease or other concurrent disease; (4) failure to respond properly to antithyroid drugs; (5) refusal of surgical or other therapy, and (6) presence of severe exophthalmos.

A contraindication for radioactive iodine therapy is coexistence of hyperthyroidism and pregnancy.

Of the 384 patients, 294 were men. Toxic diffusely enlarged glands were present in 204 patients and toxic nodular glands were present in 180. Two hundred and ninety, or 75.5 per cent, of the patients were over forty years of age.

The initial dose at the present time is 150 microcuries (new Oak Ridge standard) per estimated gram of thyroid tissue in patients under forty years of age with toxic diffusely enlarged glands, and approximately 250 microcuries in patients over forty years of age. In patients with toxic nodular glands the initial dose amounts to from 300 to 350 microcuries per estimated gram of thyroid tissue.

In patients with toxic diffusely enlarged glands the total dosage ranged from 1.8 to 59.6 millicuries with an average of 11.3 millicuries. Toxic nodular glands required an average of 20.5 millicuries to effect a remission with a range of from 3.0 to 140 millicuries.

Remissions were obtained in 76.1 per cent of the patients with one or two doses. Satisfactory remission was obtained in 372 patients (85.2 per cent), while 13.8 per cent developed varying degrees of hypothyroidism. Four patients (1 per cent) developed permanent myxedema.

Exophthalmos was noted in 114 cases and of these, in the 94 patients who were adequately evaluated, 19.1 per cent had complete regression and 58.5 per cent showed varying degrees of improvement after treatment. No progression in the degree of exophthalmos was noted when it was present prior to treatment.—*I. R. Berger, M.D.*

Seed, Lindon, and Jaffé, Bertha. Results of treatment of toxic goiter with radioactive iodine. *J. Clin. Endocrinol. & Metabol.*, Jan., 1953, *13*, 107–119.

The authors report a series of 257 hyperthyroid patients followed from six months to two years after treatment with I^{131}, with a satisfactory remission in 63 per cent; hypothyroidism occurred in 11 per cent, and in 25 per cent the results were considered to be unsatisfactory.

In 1,720 similar patients reported in the literature up to the present, a remission was obtained in 80 per cent, hypothyroidism occurred in 9 per cent and in 11 per cent the results were classified as incomplete or unsatisfactory.

Complications were very few and none were serious. Genetic injury and carcinogenic effect remain purely hypothetical possibilities.

The administration of I^{131} is the treatment of choice in recurrent diffuse toxic goiter, and in most diffuse toxic goiters in patients over forty-five years of age. Patients with large goiters are more difficult to cure and it is probably better to perform surgery. With this exception, all exophthalmic goiter patients are best treated by radioiodine.

Surgery is the treatment of choice in nodular toxic goiters, except under unusual circumstances. The operation is a satisfactory procedure, cure is certain, the goiter is removed, and complications and recurrences are rare. Cure by I^{131} is more difficult and less certain. In addition, the goiter itself rarely entirely disappears.

There are no criteria by which the dosage of I^{131} can be accurately estimated. A tracer dose is necessary. In diffuse toxic goiter the uptake is usually in the neighborhood of 70 per cent. Under these circumstances, the average patient with a small goiter can be given 6 to 8 millicuries as an initial dose. Control of symptoms can be obtained in over half the cases after the initial dose and hypothyroidism appears in another 10 to 15 per cent.

In nodular toxic goiter the uptake is lower. If it is below 20 per cent, treatment with I^{131} is not advisable under almost any circumstances. The initial dose in a patient with a nodular toxic goiter of moderate size is 20 millicuries; if the goiter is large or the symptoms severe, this can be raised to 35 millicuries. Repeated doses at intervals of two months are usually necessary. The goiter becomes smaller but does not entirely disappear, even when the hyperthyroidism is eliminated.—*Frank J. Rigos, M.D.*

Müller, J. H., and Brunner, C. Normaler Partus eines gesunden Mädchens nacherfolgreicher Behandlung einer metastasierenden Struma maligna der Mutter mittels radioaktiven Jods (I^{131}). (Normal birth of a healthy girl after successful treatment of metastasis of a struma maligna of the mother with radioactive iodine, I^{131}.) *Schweiz. med. Wchnschr.*, Jan. 17, 1953, *83*, 54–55.

A patient, seventeen years old, was operated on in 1942 for papillary adenocarcinoma of the thyroid. At operation metastases were found in several lymph nodes on the right side of the neck and removed. The operation was followed by intensive irradiation with roentgen rays.

One year later a second operation had to be carried out but the large tumor mass extended deeply into the mediastinum and could not be removed entirely. Histopathological examination again showed a highly differentiated papillary carcinoma of the thyroid.

The patient married in 1948. Early in 1949 tracer studies with I^{131} were made. The uptake in the metastatic tumor mass in the mediastinum was encouraging and a total treatment dose of 95 millicuries of I^{131} was given over a period of several months. Myxedema was produced but was satisfactorily controlled with thyrakrin.

The patient is free of symptoms $3\frac{1}{2}$ years after treatment with I^{131}; $2\frac{1}{2}$ years after treatment she gave birth to a normal child with healthy thyroid and inner organs. Birth and confinement were normal and she nursed the child.

The authors believe that this is the first case of a young woman with struma maligna and metastasis who was treated successfully with I^{131} and subsequently gave birth to a normal child.—*Otto Glasser, Xh.D.*

Jaffe, Henry L., Rosenfeld, Maurice H., Pobirs, Frederick W., and Stuppy, Laurence J. Radioiodine in treatment of advanced heart disease; end results in one hundred patients. *J.A.M.A.*, Feb. 28, 1953, *151*, 716–720.

One hundred patients with the most advanced grade of cardiac disease were treated with radioiodine and followed for at least two years. All other forms of medical treatment had failed. A multiple small dose technique was used to avoid the radiation thyroiditis with larger doses with an accompanying temporary state of hyperthyroidism and to produce a state of relative hypothyroidism while avoiding

frank myxedema. The first course of radioiodine consisted of five weekly oral doses of 6 mc. each. If response was not satisfactory at the end of an observation period of two months, a second similar course was given, and occasionally a third course after another two month interval. Forty per cent of the patients responded to one course, 54 per cent to two courses, and 6 per cent required three courses. In evaluating the response, it was found that the basal metabolic rate and the protein-bound blood iodine level were not always reliable. Radioiodine uptake thyroid studies were found to be the most accurate index of thyroid function. If any indication of myxedema supervened, small doses of thyroid extract were prescribed. Since it was found that the normal thyroid gland might recover its function months after radioiodine treatment, patients were tested every two to three months.

Results of the treatment were classified as 53 per cent good, 20 per cent fair, and 27 per cent poor. Included in the latter group were 24 patients who died during the study. Of these, 33 per cent showed a good result and 25 per cent a fair result prior to death. No untoward effects were observed following the treatment. Patients rarely complained of thyroiditis, and when this occurred it cleared up in a few weeks. There was no evidence of bone marrow depression nor radiation sickness. It is concluded that the treatment is useful in patients with severe cardiac disease who have failed to respond to all other types of medical management.—*Leslie K. Sycamore, M.D.*

STIRRETT, LLOYD A., YUHL, ERIC T., and LIBBY, RAYMOND L. A new technique for the diagnosis of carcinoma metastatic to the liver; a preliminary report. *Surg. Gynec. & Obst.*, Feb., 1953, *96*, 210–214.

It is the purpose of this article to describe a new technique which employs abdominal radioactivity surveys for the detection of carcinoma metastatic to the liver. According to Satterlee, the liver is the seat of blood borne metastases in 36 per cent of all cases of cancer, 44 per cent of all cases of gastric carcinoma, 50 per cent of all cases of carcinoma originating in portal areas, and 48 per cent of all cases of breast cancer.

The various hepatic function tests and needle biopsy of the liver are the only laboratory means currently available to the clinician. These methods are unreliable, however, when dealing with early or solitary hepatic metastases.

The technique described involves the use of radioactive iodinated human serum albumin (I*HSA) as the tracer material and the scintillation counter as the detector of the gamma radiation from the I^{131}.

Method. Each patient is given a single sterile intravenous injection of 300 microcuries of I*HSA. The survey is made twenty-four hours later. About 5 per cent of the radioactive iodine contained in the I*HSA may be absorbed by the thyroid gland. In order to prevent assimilation of this iodine and to preclude an untoward effect upon thyroid function, 0.5 cc. of Lugol's solution is given t.i.d. prior to the survey and six days thereafter.

Summary

1. Fifty-six patients were studied by this method and the findings were correlated with those of conventional liver function tests and the operative findings.

2. An over-all diagnostic accuracy of 96 per cent was obtained in this preliminary series.—*Mary Frances Vastine, M.D.*

MONEY, WILLIAM L., FITZGERALD, PATRICK J., GODWIN, JOHN T., and RAWSON, RULON W. The effect of thiouracil on the collection of radioactive iodine in experimentally induced thyroid tumors. *Cancer*, Jan., 1953, *6*, 111–120.

Thiouracil was given to Sprague-Dawley strain rats for varying lengths of time. It was found that a long period of treatment—in the vicinity of 500 days or more—was required to produce thyroid tumors in 100 per cent of the strain used. Twenty-four hours before autopsy, I^{131} was given to rats which had been maintained on thiouracil and were continued on thiouracil until autopsy. In 11 of the 81 rats studied, no evidence of I^{131} was found in the radioautographs of the thyroid gland. In 7 of these, no significant lesions were found—only characteristic thiouracil effect. Thirteen rats showed radioactivity in areas of the thyroid not containing lesions. Generally, the radioactivity was found in the colloid of the peripheral follicles more than in the central follicles. In some instances where I^{131} was found in the peripheral follicles, none was found in the central follicles.

The concentration of I^{131} in the thyroid gland of treated rats was considerably lower than in the controls and nearly all was inorganic as opposed to the organically bound I^{131} in the controls.

The authors state that uptake of I^{131} by tumors and abnormal follicles suggests an escape from the normal blocking action of thiouracil. The most likely explanation for this is that the doses necessary to block such areas may differ greatly from that which inhibits normal thyroid.—*John P. Storaasli, M.D.*

MCLAREN, H. C., HEATH, J. C., and QUINTON, A. Radioactive phosphorus (P^{32}) in treatment of menorrhagia. *Brit. M. J.*, Feb. 14, 1953, *1*, 358–363.

Menorrhagia persisting after curettage in women over forty years of age always raises the question of treatment by irradiation or surgery. Radiation castration may be accompanied by menopausal symptoms and premature age effects. Surgery with ovarian conservation may avoid sequelae, but carries a

small but definite mortality and morbidity. For these reasons, the authors have attempted to avoid radical treatment by cauterizing the endometrium with beta radiation.

The applicator consisted of a plastic cylinder 4.5 cm. in length and 1 cm. in diameter. Filter paper saturated with an aqueous solution of sodium hydrogen phosphate in which the phosphorus was radioactive P^{32} was molded over the cylinder and the whole covered with a thin plastic sheath. A Y applicator was also used in some cases. Animal experimentation on the rabbit vagina was carried out as a preliminary step.

Initially, 4 patients scheduled for hysterectomy and bilateral salpingo-oophorectomy were treated with the applicator and then the operation performed within twenty-one days. Subsequently, 11 more patients were treated and three months were allowed to pass before hysterectomy. Patients experienced no significant discomfort or radiation sickness.

Of the 11 patients treated and observed for three months, improvement as judged by the onset of amenorrhea or normal menstruation was achieved in 8. One was improved for two periods and then relapsed. Two patients with unsuspected fibroids of the myometrium were failures.

Pathological examination revealed necrosis of the endometrium to a depth of 1.5 to 2.0 mm., with the deeper layers severely damaged by the usual radiation changes. The deeper glands and stroma nearest to the myometrium appeared to escape irradiation injury and regeneration of endometrium followed. After three months, the surface epithelium occasionally showed marked irradiation distortion and below the surface a waxy or hyalin appearance of the stroma was observed. The ovaries, as would be expected, were not affected.

Apparently no more than a temporary hemostasis can be expected by this method, but this might be valuable in certain instances and the results suggest that menstruation when re-established might be normal. The possibility of carcinogenic action on the affected endometrium must be kept in mind and can be answered only by observation over a sufficient length of time. The possibility of fetal abnormality through implantation on damaged tissue is a theoretical objection, but seems a very remote probability.

The quantity of P^{32} employed for application varied from 2.72 mc. to 4.75 mc. The applicator was left in for periods varying from 57 to 152 hours. Absorption experiments in wax indicated that the surface dose varied from 110,000 rep to 265,000 rep and the estimated depth of cauterization varied from 2.3 mm. to 3.0 mm.—*Leslie K. Sycamore, M.D.*

KING, E. R., MASON, M. W., MESSINGER, H. B., and DUDLEY, H. C. A preliminary report on the use of gallium^{72} in clinical tracer studies. *Radiology*, Dec., 1952, *59*, 844–848.

Clinical tracer studies using 500 microcuries of gallium 72 demonstrated increased gallium localization in 8 out of 14 patients having definite bone metastasis. Eight out of 11 patients having advanced hypertrophic arthritis showed increased deposition of gallium in the region of the osteophytes. Hence gallium 72 does not appear too promising as a diagnostic tool, although further studies are necessary for conclusive results.—*Martin B. Goodwin, M.D.*

ODEBLAD, ERIK. Artefacts in autoradiography. *Acta radiol.*, March, 1953, *39*, 192–204.

The author had the opportunity to examine more than ten thousand autoradiographic negatives prepared with different techniques and using a variety of isotopes such as P^{32}, S^{35}, C^{14}, Se^{75}, Cd^{115}, and several members of the thorium series. About one-half of these negatives exhibited minor or major artefacts.

In the present article he analyzes in detail the various sources of the artefacts and based on the observations made suggests concrete measures for their prevention.

The following five techniques were employed in this work: (1) the separation technique, in which the histologic section is brought in contact for a certain length of time with a sensitive film then separated and the latter developed; (2) the coating technique, in which the emulsion is painted directly on the histologic section, the emulsion and section thus being in close contact during the photographic and histologic processing; (3) the stripping film technique, in which a thin emulsion on a gelatin or celluloid base is floated on water with its sensitive side downwards and is then lifted from the surface of the water with a slide containing the histologic section on it; (4) the mounting technique, in which the histologic section is mounted directly on the photographic plate; and (5) the Boyd and Levy modification of this latter. Other known techniques such as the inverted autograph technique of Bélanger, the wet process technique of Gomberg and the focussed autoradiography of Marton and Abelson are not considered.

The artefacts may result from such varying sources as (1) the method of administration of the radioactive isotope (improperly selected amount of carrier material, accidental formation of colloidal aggregates, contamination with other isotopes, etc.); (2) the histologic treatment of the section; (3) the variation in the sensitivity and thickness of the emulsion and flaws in its manufacture; (4) the interferences occurring during exposure (pressure contact, friction induced sparks, luminescent effect, chemical pseudophotographic interaction, etc.); (5) the photographic processing, and (6) some other sources, as for example, uneven graininess of the photographic emulsion, accumulation of dirt or dust on the film before exposure and careless photographic hygiene.

The author emphasizes that in interpreting autoradiographs the findings should not be regarded as final until confirmed on several films and, prefer-

ably, in several specimens. He concludes by recommending the following important preventive measures: (1) use of clean radioisotope solutions; (2) careful choice of histologic fixing agents; (3) meticulous histologic mounting; (4) avoidance of touching the emulsion surface with the fingers; (5) application of only moderate pressure during exposure; (6) prevention of mechanical injury of the film during the wet processing; (7) use of fresh and clean filtered solutions for development and fixation; (8) scrupulous avoidance of dust; (9) procuring of control sections without radioisotope exposure; and (10) observation of spotless cleanliness in the dark room.

The article is well illustrated with autoradiographic reproductions showing artefacts of all categories discussed. A bibliography of 32 articles is appended. —*T. Leucutia, M.D.*

MYANT, N. B. Prognostic value of early tests of thyroid function after treatment of thyrotoxicosis by ^{131}I. *Brit. J. Radiol.*, March, 1953, *26*, 139–143.

Estimation of the magnitude of the dose to be administered is one of the difficulties in the treatment of thyrotoxicosis with I^{131}, especially if the single dose method is used. Many workers prefer the fractionated method which permits a gradual adjustment of the dosage by the addition of successive small amounts until the desired effect is obtained. The disadvantage of this procedure is the long delay between each fraction of the dose due to the fact that the clinical response may not become apparent until some time after the critical radiation dosage has been delivered to the thyroid.

Aiming to devise a more rapid assay of the clinical response, the author studied in a series of 25 patients who received 36 treatments the radioiodine uptake of the thyroid shortly after each treatment and related the results obtained to the patient's subsequent clinical course. The N/T (neck/thigh) ratio, or the ratio of the counting rate at 60 cm. from the front of the neck to the counting rate at 7 cm. from the surface of the thigh, was used as a test of the radioiodine concentrating activity of the thyroid, the counting rate over the thigh indicating the plasma concentration of the radioiodine. This test was performed once or several times before treatment (at two hours after intravenous injection of 100 microcuries of I^{131}) then three weeks after the administration of the treatment dose (by using a somewhat larger amount, up to 530 microcuries, for the test) and again each time the patient reported for the clinical follow-up. If radioiodine was already present in the body from earlier tests or from the treatment dose when the N/T ratio determination was undertaken, the necessary correction for this residual radioactivity was made. This procedure is decribed in detail.

The results of the tests are tabulated for all 36 treatments by indicating: (1) the dose in millicuries; (2) the N/T ratio before treatment; (3) the N/T ratio three weeks after treatment (percentage of pretreatment value); (4) the clinical response; (5) the N/T ratio at follow-up (percentage of pretreatment value); and (6) the radiation dose to thyroid in three weeks, expressed in e.r. The significance of the figures obtained is discussed at length.

Briefly, the conclusion is reached that the thyroid function shows greater inhibition at three weeks after administration of a therapeutic dose of I^{131} than at later intervals. Remission is unlikely to occur unless there is significant depression of the thyroid function at this interval, but not every depression is necessarily followed by a remission. In some instances the thyroid function remained at, or returned to, an abnormally high level although clinically the patients exhibited remissions. This anomaly needs further experimental clarification.—*T. Leucutia, M.D.*

STEPHENS-NEWSHAM, L. G. The measurement of radioactive iodine in vivo. *J. Canad. A. Radiologists*, March, 1953, *4*, 20–22.

The gamma emission of I^{131} may be detected externally by Geiger counters. If a given counter is calibrated with a known source and then used to measure the amount of radioactivity in the thyroid gland, the distance to the thyroid gland must be known so as to rule out errors due to distance.

Multiple counter arrangements of from two to four counters have been used by various workers. This eliminates error due to position of the gland but has drawbacks in that the patient must be in the sitting position and high background counts are difficult to obtain. Errors due to scattered radiation also occur, giving a higher count than that actually due to the I^{131} present in the gland.

The author describes a two counter arrangement which eliminates the usual drawbacks of multiple counter measurement of total radioactive iodine uptake of the thyroid gland. He determined the correction necessary for scatter and absorption by phantom studies and found this to be 8 per cent for average sizes of necks. He also describes a directional lead-walled counter and gives figures depicting its characteristics.—*R. W. Emerick, M.D.*

LEHMANN, JUSTUS, GOSPOS, HEDI, and NITSCH, WILLI. Untersuchungen über die Permeabilität verschiedener Erythrocyten für radioaktiven Phosphor bei der durch Immunkörper bedingten haemolytischen Anaemie. (Investigations of the permeability of various erythrocytes to radioactive phosphorus in immunologically induced hemolytic anemia.) *Strahlentherapie*, 1953, *89*, 573–579.

The injection of rabbit immune amboceptor into guinea pigs produced hemolytic anemia. The permeability of erythrocytes, especially the microsphero-

cytes and macroreticulocytes, to the inorganic, radioactive phosphorus was investigated in these animals.

The microspherocytes were more permeable to *entrance* of the phosphorus than were the normocytes or macroreticulocytes. Permeation time *out* of the cells, however, was the same for all erythrocytes. This is attributed to the phosphorus entering into organic combination within the cell and being released so slowly that the permeability of cell membrane is not the determining factor.—*Henry G. Moehring, M.D.*

Hiller, Johannes, Jakob, Alfons, and Strauss, Ernst. Zur Analyse des normalen und des pathologischen Eisenstoffwechsels mit Radioeisen. (Analysis of normal and pathologic metabolism of iron with radioactive iron.) *Strahlentherapie*, 1953, *89*, 596–599.

The metabolism of iron in normal and abnormal states is demonstrated with radioactive iron. In anemias secondary to bleeding, iron metabolism is accelerated; in anemias secondary to infections it is slowed down.

Recent biochemical investigations of iron metabolism indicate a possible connection of these phenomena with protein metabolism.—*Henry G. Moehring, M.D.*

Barnes, Allan C. Experimental nonsurgical therapy of pelvic malignancies; a review. *Am. J. Obst. & Gynec.*, March, 1953, *65*, 550–559.

A group of experimental suggestions and trials that have been made in therapy of pelvic malignancies are reported. Since none of these are five years old, there are no five year cure rates. The nature and limitations of cobalt 60, gold 198, intra-arterial nitrogen mustard and intravenous progesterone are evaluated.

The main advantages cobalt offers are adaptability to the individual patient, and/or the patient's tumor. It must be stressed that this is gamma radiation; if a patient is at tolerance to roentgen rays and radium, she is at tolerance to cobalt. The tumor that is being irradiated does not distinguish whether the gamma ray that strikes it is coming from radium, cobalt, or from any other source. This, then, is not going to extend any additional therapy to the patient who is at tolerance. Rather, it represents an individualization and a potential way to individualize the patient which is not available if we are harnessed to sources which are regrouped and rearranged only with some hazard and at considerable effort and expense to the institution.

The characteristics of radioactive gold are in sharp contrast to those of cobalt. It has a half-life that is exceedingly brief, 2.7 days, which immediately presents dosage and transportation problems. It produces gamma rays, which are soft, and it has a beta ray which is comparatively strong. As with the other metals, leakage is impossible. In a finely ground state, it is easily handled in colloidal solution. Gold can be activated in any desired shape, at an exceedingly moderate cost, and in any quantity. It is also physiologically inert, and can be successfully injected into the body. Sherman introduced the interstitial injection of colloidal gold mixed with pectin. The injection is made directly into the parametrial tissues; the active particles are picked up in the lymphatics and carried to the nodes. There is perhaps no more logical way of reaching the pelvic lymph nodes than to have the lymphatics carry the radiation there.

Nitrogen mustard administered into the blood stream will attack the first surface it goes by. If it is put in a vein, one treats the bone marrow and the pulmonary stystem. If it is put into the arterial side, it will go into the first epithelial surface that it passes on being distributed through the capillary bed. That immediately means that the gynecologist should be interested in it, because the arterial system to the pelvic malignancies is relatively localized, and readily accessible.

In 1951 Hertz suggested the use of progesterone in cancer of the cervix, and has reported the histopathologic changes in squamous cell cervical carcinoma after massive doses of progesterone. The recommended minimum dose is 250 mg. of progesterone a day, and many of the courses lasted up to 100 days. On sequential biopsies during progesterone therapy, there is a tissue change in the malignancy. In 25 per cent of one series the biopsy turned negative. In 33 per cent the positive Papanicolaou smear was reversed. The negativity in each case was temporary. No patients were cured.—*Eugene J. McDonald, M.D.*

Hahn, P. F., and Carothers, E. L. Lymphatic drainage following intrabronchial instillation of silver-coated radioactive gold colloids in therapeutic quantities. *J. Thoracic Surg.*, March, 1953, *25*, 265–279.

This paper discusses the distribution of silver-coated radioactive gold particles at levels of radioactivity judged to be in a therapeutic range for bronchiogenic carcinoma after their intrabronchial administration in dogs.

It was found that the silver coat, which is also radioactive, assists in the transport of the radioactive gold nucleus by way of the lymphatics to the peribronchial and mediastinal lymph nodes, thus irradiating these common sites of metastases. The silver, in promoting the relatively rapid transfer of the radioactive gold to the lymphatics, helps protect the lung from an inordinate amount of irradiation. The silver coat is gradually leached off in the lung and carried to the liver for secretion, probably by the biliary tract.

Estimated dosage to the liver is felt to be within tolerable limits by a factor of approximately ten times. Dosages to the thoracic lymph nodes are estimated to be of the order of several hundred thousands equivalent beta roentgens. No uniform distribution of the radioactive particles in the lymphatics was found but this discrepancy would probably be compensated by the fact that in most cases doses many times the cancerocidal dose were used. The problem of tumor obstructing the lymphatics and hence the passage of therapeutic radioactive substance is considered and it is suggested that collateral lymphatic drainage may come to the aid of the therapist.—*Paul C. Olfelt, M.D.*

FREUNDLICH, H. F., and HAYBITTLE, J. L. An improved iridium-192 teletherapy unit. *Acta radiol.*, March, 1953, *39*, 231–240.

An Ir^{192} teletherapy unit has been used continuously at Addenbrooke's Hospital, Cambridge, England, since May, 1950. Owing to the fact that Ir^{192} has a half-life of only 74 days, two identical sources were provided, one being activated in the pile at A.E.R.E., Harwell, while the other was in use in the unit. The two sources were interchanged every four weeks. A full account of the design and construction of this unit has been given previously (see Abstr. this JOURNAL, 1951, *66*, 164).

In the present article the authors report on an improved unit having a higher output and greater flexibility. They describe in detail the design and construction of this new unit as well as the loading and unloading procedures of the Ir^{192} source and give some additional data of physical measurements.

The maximum output of this new unit is 27.5 roentgens per minute at 9 cm. source-skin distance, or 14 roentgens per minute at 13 cm. source-skin distance, the two most commonly used distances in clinical therapy. The mean energy of the gamma rays emitted is 400 kev. It was determined that the central axis depth dose curves of a 7 cm. diameter field when treating at 25 cm. source-skin distance compare favorably with those of roentgen rays of 1.5 mm. Cu half-value layer, using a similar size field and a focus-skin distance of 50 cm. The output of the unit at 25 cm. is too small to be of any practical value at present, but it is quite probable that sources of higher initial density will become available soon. The authors, therefore, believe that the possibilities of wider use of the Ir^{192} are worthy of consideration until sufficient quantities of $cesium^{137}$ will be ready at Oak Ridge for construction of larger teletherapy units.

The authors have also made a series of protection measurements. The unit is installed in a room originally planned for a 220 kvp. roentgen therapy apparatus, the operator's cubicle being lined with lead of 6 mm. thickness. The maximum dose rates recorded anywhere were found to be within permissible limits. Dental films strapped to various points of the treatment head showed that, with the unit switched off, the maximum dose rate was 0.07 roentgen per hour and at the nozzle when the applicator was removed it was 0.7 roentgen per hour. These dose rates are considered safe, assuming that the operator's hands will never be in contact with the head of the unit for more than five hours or in the nozzle region with the applicator removed for more than half an hour during any working week.—*T. Leucutia, M.D.*

CHEMOTHERAPY

HERVÉ, A., and BACQ, Z. M. Protection chimique contre le rayonnement X (essais thérapeutiques). (Chemical protection against the x-radiation; therapeutic attempts.) *J. de radiol. et d'électrol. & Arch. d'électric. méd.*, 1952, *33*, 651–655.

In the introduction the authors give a brief résumé of the symptomatology, pathogenesis and the presently used methods for the treatment of radiation sickness.

Since 1949, the Liége Section of the Belgian National Center of Growth, stimulated by Bacq, has undertaken a series of experimental investigations on the problem of chemical protection against the roentgen rays. It was demonstrated that several substances produced survival of mice from a lethal dose of roentgen rays, provided they were injected immediately before irradiation.

Among these, β-mercapto-ethylamine ($HS.CH_2.CH_2.NH_2$) which is a decarboxylation product of cysteine gave the most encouraging results. Thus a single intraperitoneal injection of 3 mg. before irradiation was sufficient to save 97 per cent of the mice from the lethal dose of 700 r and 30 per cent of the mice from the even larger dose of 900 r which killed all the control animals within four days. The authors give a tabular compilation of all amines which proved useful by indicating the comparative rates of survival which were obtained by injecting an equimolecular dose of 3 mg. of cysteine-amine.

In view of this marked protective effect and since the substance is only mildly toxic, it was decided to use β-mercapto-ethylamine, designated with the symbol of 1573 L, also in clinical therapy to combat radiation sickness. Thirty patients were chosen who received large daily doses of roentgen rays and who had already developed radiation sickness to a degree that would have necessitated interruption of further treatment. The radiation sickness consisted in the main of gastrointestinal manifestations, such as anorexia, nausea, vomiting and diarrhea. Uniformly, a dose of 200 mg. was given intravenously (the intramuscular injection often proving very painful). The results obtained in the 30 cases are presented in a tabular form by listing the sex, age, diagnosis, irradiated region, the symptoms before and after the

administration of the drug, and the number of injections and time of disappearance of the symptoms.

The following observations were made: (1) the radiation sickness, and in particular its gastrointestinal component, diasppears under the influence of one or several injections of β-mercapto-ethylamine; (2) a single dose suffices in the majority of instances, although occasionally the treatment may have to be continued for forty-eight to seventy two hours before the desired effect is obtained; (3) not a single failure was noted in the entire series and often the effect was dramatic; (4) in those cases requiring prolonged irradiation with large doses of roentgen rays sometimes it was found necessary to repeat the injection of the drug after six to ten days.

The authors now treat systematically all cases of radiation sickness with β-mercapto-ethylamine and, although they are not prepared as yet to draw final conclusions, they believe that the method has surpassed the experimental stage. They have not used the drug on a prophylactic basis but it is quite possible that such procedure might prove of distinct value.—*T. Leucutia, M.D.*

Marshall, A. H. E. The action of cortisone on experimental acute roentgen dermatitis. *Acta radiol.*, Jan., 1953, *39*, 73–77.

Sensitivity of cells to ionizing radiation is in part dependent on their proliferation rate and metabolic activity. Green and Ghadially claim that cortisone inhibits cell division in the normal epidermis, and might be expected together with the general anti-inflammatory action, to affect the development and course of acute radiation reaction of the skin. The failure of Smith *et al.* to influence with cortisone or ACTH the mortality of mice subjected to whole body roentgen irradiation may possibly be due to lack of inhibition of cell proliferation in the normal bone marrow by either hormone.

One hundred and seventy mice of two separate strains were used, one strain for irradiation of the body skin and the other, a hairless recessive strain, for irradiation of the tail. The factors employed were 60 kv., 4 ma., 3 cm. distance, H.V.L. of 2.8 mm. Al and an output of 408 r per minute. Cortisone was injected under two schedules, the first schedule being applied just prior to and during the course of irradiation, and the second after irradiation and until ten days after the reaction had developed. The control animals received an equivalent volume of normal saline.

The naked eye appearance of the reaction under the cortisone treatment was considerably modified, the edema, erythema and oozing of serum from the skin surface, seen in the normal animal, being absent or diminished and replaced by a relatively silent and less acute process. Healing appeared to proceed normally under cortisone treatment.

The results indicate that cortisone considerably delays the onset of acute radiodermatitis and restricts the area of damage produced when measured in a given period from its onset. Better results are obtained when cortisone treatment is commenced shortly before the appearance of the skin reaction and continued throughout its course.—*John R. Smith, M.D.*

Hallberg, O., Nohrman, B., and Sylvén, B. Survival time in women with disseminated breast cancer, following testosterone treatment. *Acta radiol.*, Feb., 1953, *39*, 161–168.

Although the palliative effects of androgen therapy in women with disseminated breast cancer are poorly understood, the clinical course in some cases may be retarded or accelerated by androgens as well as by estrogens. The authors' article presents data on the alleged influence of androgen treatment on the length of survival time in women with skeletal metastases from mammary cancer. All cases showing unequivocal signs of visceral involvement at the time of onset of bone metastases have been excluded, since the results with androgen treatment in these cases have largely been disappointing and, furthermore, in most instances it was impossible to accurately estimate the extent of visceral deposits.

From a total of 254 verified cases of mammary cancer with skeletal metastases, 97 were treated with androgens; 57 of the 97 cases were post-menopausal, and 40 belonged to the child-bearing age. Of the latter, all but 4 had previously undergone castration by irradiation. All cases continuously received intramuscular injections of testosterone propionate according to a previously described regimen, the average dose being 225 mg. per week until subjective improvement was obtained and then changed to 150 mg. weekly as a maintenance dose.

A significant increase in survival time was found in the androgen treated series during the first to the end of the fourth year after the onset of skeletal metastases, the relative increase of survival being most marked in the post-menopausal group. In the fertile group, neither roentgen castration alone nor castration plus testosterone had any significant influence on the survival rate. The mean survival time from the onset of skeletal metastases was twenty-one months in the androgen series, as compared to fifteen months in the control series. In the post-menopausal group the corresponding figures were twenty-two and thirteen months, respectively. No significant increase in the survival time could be demonstrated in the fertile group of women.—*John R. Smith, M.D.*

Robbins, Jacob John, and Lyons, William F. Beryllium granulomatosis; report of a case showing response to cortisone. *Ann. Int. Med.*, Jan., 1953, *38*, 120–124.

The authors describe the case of a female patient who, eight years after beryllium exposure in Ohio,

developed signs and symptoms of respiratory failure secondary to chronic pulmonary fibrosis of the beryllium granulomatous type. The roentgen findings in the chest were very marked. The patient declined in weight from 210 pounds to 89 pounds and was extremely dyspneic.

She was given 200 mg. of cortisone daily. Improvement started on the third day; on the fifth day cough and dyspnea had almost completely disappeared and oxygen was discontinued. Vital capacity increased from 300 cc. to 1,000 cc. and the patient was able to get out of bed. The dosage of cortisone was gradually reduced until it was found that she could be maintained on 25 mg. daily. This has been continued for twelve months. In spite of the dramatic clinical improvement which this patient manifested the roentgen changes in the lungs remained essentially the same.—*C. L. Hinkel, M.D.*

PATERSON, EDITH, KUNKLER, P. B., and WALPOLE, A. L. Triethylene melamine in human malignant disease; results with oral administration of enteric-coated tablets. *Brit. M. J.*, Jan. 10, 1953, *1*, 59–64.

This report summarizes the experimental and clinical background for the drug known as triethylene melamine or T.E.M. in the United States and as trisethyleneimino-s-triazine or 9500 in the British Isles.

The authors conducted animal experiments to compare effectiveness of intraperitoneal, intravenous and parenteral routes of administration. When given by mouth 50 times the parenteral dose was needed to produce a comparable effect T.E.M. is unstable to acids and this seems to account for the variability in degrees of inactivation in the stomach.

Clinical trials in 43 patients were also conducted. Oral administration of the drug in the form of enteric-coated tablets gave a reasonable consistency between dose and effect. Carcinomas and sarcomas did not respond appreciably to this therapy. Hodgkin's disease and chronic leukemias showed, in general, worth while responses. Of chronic leukemic patients, the lymphatic group responded better than did the myelogenous. Dosages of 0.2–0.3 mg./kg. as one dose or within a two or three day interval seemed optimal for lymphoma. Dosages of 0.1–0.2 mg./kg. were found adequate for the leukemias.

T.E.M. therapy should not be instituted in patients who already have leukopenia from earlier therapy. Repetition of treatment is possible, provided the polymorphonuclear count can be fully restored. Hepatic and renal tolerances for toxic effects of T.E.M. were found to exceed the tolerance of the hemopoietic system. Close hematological control is essential in any plan for use of this agent.—*John W. Turner, M.D.*

MISCELLANEOUS

RITTER, VERN W., WARREN, S. REID, JR., and PENDERGRASS, EUGENE P. Roentgen doses during diagnostic procedures. *Radiology*, Aug., 1952, *59*, 238–251.

Using 14 diagnostic units, air dose rates were determined at various distances and voltages and with different degrees of aluminum filtration. For a given set of factors, the dose rates from the 14 different machines were averaged.

Variations in measured outputs were as great as plus or minus 20 per cent of the average values, hence a safety factor of 1.2 times the average was used when the pertinent data were plotted. From these data, curves were set up so that the skin, depth, and integral volume doses may be calculated for any diagnostic machine for any diagnostic procedure, provided that this machine has been standardized to these curves by at least one dose determination. The calculated dosages are in extremely close agreement with other published results. Skin and depth doses for the diagnostic techniques used at the University of Pennsylvania Hospital are given in tabular form.—*Martin B. Goodwin, M.D.*

BECKER, J., SCHEER, K. E., and KÜBLER, A. Ein neues Strahlenmessgerät mit einer biegsamen Kristallmessonde und seine Anwendung in der Klinik. (A new radiation meter with a flexible sound containing the measuring crystal and its clinical use.) *Strahlentherapie*, 1952, *88*, 34–43.

A new device for measuring radiation is based on the principle that the conductivity of a cadmium sulfide crystal varies under the influence of ionizing radiation. The entire apparatus is small and the tip which picks up the radiation is flexible so the device is particularly suited to measurement of radiation from radium or other gamma emitters and plotting isodose curves about irregularly shaped radiation sources.—*Henry G. Moehring, M.D.*

BROOKS, JAMES W., EVANS, EVERETT IDRIS, HAM, WILLIAM T., JR., and REID, J. DOUGLAS. The influence of external body radiation on mortality from thermal burns. *Ann Surg.*, Sept., 1952, *136*, 533–545.

Among the victims of the atomic bomb attacks on Hiroshima and Nagasaki, it was found that those in the intermediate zone of combined radiation and thermal injury suffered a mortality from burns which was so high as to make it difficult to explain on the basis of thermal injury alone, although the radiation dosage was not high enough to be lethal. The authors, therefore, studied the effects of minor external body radiation injury inflicted at the same time as moderate thermal injury.

Five groups of dogs were used in the experiment. Group A received a standard 20 per cent contact burn alone; Group B, 100 r external body radiation alone; Group C, the 20 per cent burn plus 25 r

external body radiation; Group D, the 20 per cent burn plus 100 r external body radiation; and Group E penicillin therapy in addition to the combined thermal and radiation injury. Some of the dogs receiving the combined injury were given the thermal lesion first, and then exposed to the roentgen-ray dose. Others were treated in reverse order. The order of procedure did not appear to produce detectable differences. Extensive laboratory studies were conducted on each dog including hemoglobin determination, hematocrit, red blood cell count, white blood cell and differential counts, total plasma proteins, plasma volume, bone marrow studies, blood cultures, wound cultures and wound healing time.

In Group A the mortality was 12 per cent; in Group C, 20 per cent; and in Group D, 75 per cent. Dogs in Group B receiving 100 r of radiation alone showed no significant effects.

The dogs in Group D which died succumbed to septicemia due to beta hemolytic streptococci. It appeared that radiation depressed phagocytic activity and other defense mechanisms to a point where they were unable to localize the streptococci at the wound surface. When daily intramuscular doses of 900,000 units of crysticillin were given to the Group E dogs, which had received the combined thermal and radiation injury, the mortality was reduced to 14 per cent, indicating the importance of this therapeutic measure in the treatment of victims of atomic bomb attack.—*Leslie K. Sycamore, M.D.*

Plough, Harold H. Radiation tolerances and genetic effects. *Nucleonics*, Aug., 1952, *10*, 16–20.

This article is a brief review of an important aspect of radiobiology. An involved discussion of acute and chronic tolerance levels of various mammals is given. The maximum permissible chronic level which is safe for humans has been placed at 0.3 r per week by the International Commission of Radiological Protection. The author points out that dosages of this magnitude will result in 15.6 r in one year and 156 r in ten years. He then reviews the exposures that an individual receives during routine roentgenological procedures and says that he feels this may possibly represent a greater potential hazard to the population in general than the exposure of a small fraction of the population to the radiation effects from atomic explosions.

The genetic effect of irradiation appears to be additive and from data on *Drosophila* and mice, conclusions are drawn on their possible long term effect on the human race. For comparison, the author assumes that the increase in spontaneous mutation rates in mice following irradiation is the same for humans. On this assumption, 80 r and possibly as little as 30 r would double the human spontaneous mutation rate.

It is hoped, the author states, that the foregoing facts and figures will indicate that radiation hazards cannot be neglected for human beings, even though they are not immediately apparent to the individual receiving the exposure.—*John P. Storaasli, M.D.*

Ting, T. P. A method for quantitative evaluation of the effects of ionizing radiations on growth of adenocarcinoma *in vivo*. *Science*, Aug. 8, 1952, *116*, 149–151.

Determining quantitative biological effectiveness of various types of ionizing radiations on experimental tumors is a difficult and tedious undertaking which is often wrought with considerable statistical error.

A new and relatively simple method, based on earlier work by Blum, is described by the author. This work utilizes the knowledge that tumors transplanted by the usual methods and measured periodically by calipers, grow at a constant rate until a certain over-all size is reached, at which time the rate deviates from that expected. Irradiated tumors were also found to grow at a constant but reduced rate, with the reduction from normal increasing as the amount of ionizing radiation to the tumor is increased. Thus it is possible to give small sublethal doses of ionizing radiation of various types and by comparison of their early growth rates to determine their relative biological effectiveness. A simple formula is proposed by the authors for this determination.

One major advantage of this method is the ability to measure the effects produced by a dose of radiation far below that required for a lethal effect. This is especially true when dealing with very resistant tumors.—*John P. Storaasli, M.D.*

Kalmus, H., Metrakos, J. D., and Silverberg, M. Sex ratio of offspring from irradiated male mice. *Science*, Sept., 12, 1952, *116*, 274–275.

Mutation, sperm lethality, sterility (semi or total), and reduction in litter size have been reported as a result of roentgen irradiation of mice (male or female). This paper, a preliminary report, deals with and briefly analyzes litter size.

Twenty-pairs of A/HeJax mice formed the experimental group. Two litters were first allowed each pair. The parents were separated shortly before the birth of the second litter. Within twenty-four hours of this birth the males received 150 or 300 r to the genitalia (no factors given) and were then returned to their mate. The third litters (born within forty days of the irradiation date) were compared with the first two litters born before irradiation. A control consisted of three generations of nonirradiated mice. No figures are given concerning differences in results of 150 and 300 r.

Results from the above indicate that reduction in litter size is due to decrease in the number of females in the postirradiation litters. In all studies, the male

totals showed no significant variation.—*P. B. Parsons, M.D.*

LORENZ, W. Hämatologische Untersuchungen über die Cystein wirkung. (Hematologic investigations of the effect of cysteine.) *Strahlentherapie*, 1952, *88*, 190–197.

Cysteine injected intracardially into rats before giving them 800 r total body irradiation raised the survival rate from 10 per cent to 75 per cent. The surviving rats showed the same hematologic damage as irradiated controls that had not received cysteine.

Adrenalectomy increased radiosensitivity of the animals and decreased the protective effect of cysteine.—*Henry G. Moehring, M.D.*

REID, THOMAS R., and GIFFORD, MARGARET P. A quantitative study of the effects of X radiation on cells *in vitro*. *J. Nat. Cancer Inst.*, Oct., 1952, *13*, 431–439.

Tissue cultures have been used for some time in studying the effects of ionizing radiation. A preparation of "replicate" tissue cultures and the quantitative determination of the number of viable cells in each culture is the method employed by the authors. The method is described in detail.

The culture medium is placed midway between two roentgen tubes 50.5 cm. apart. The factors are as follows: 186 kvp., 20 ma., 0.5 mm. Cu plus 0.25 mm. Al, and a dose rate in air of 380 r/minute.

The cell nuclei are counted quantitatively and this technique is described. It was proposed to analyze the dose-response pattern with a varying dose technique to arrive at a base line for future radiation physiology experiments.

Doses of 2,000 r, 1,000 r, 750 r, 500 r, and 250 r were given.

At 2,000 r there was an arrest of growth during the first twenty-four hours with a slow gradual decline in the population until at thirteen days 50 per cent of the cell population was dead. At forty-eight hours the nuclei were swollen and poikilocytotic. Mitoses could not be recognized.

At 1,000 r the cultures proliferated for four to five days in a slow manner with a fall-off at five days until at the thirteenth day only 50 per cent of the total population was living.

At 750 r the response was so variable that curves could not be accurately drawn up. It was concluded that 33 to 50 per cent of the total cell population will survive such a dose.

At 500 r and 250 r all the cell colonies survived.

The authors conclude that a dose of 1,000 or 2,000 r is lethal and that a dose of 750 r is partially lethal. Doses of 250 to 500 r are followed by recovery.—*Frederick W. O'Brien, Jr., M.D.*

WENTWORTH, JOHN H., and BILLOWS, JOHN A. Synergistic action of cortisone and total-body irradiation in mice. *Radiology*, Oct., 1952, *59*, 559–563.

In view of the fact that laboratory evidence indicates that both ionizing irradiation and cortisone inhibit the sulfhydryl obligate enzyme systems, the authors were interested in investigation of the possible synergistic action of these two therapeutic agents.

Small groups of 12 to 15 white male inbred mice were used for the test subjects. A single dose of 400 r (including backscatter) with 220 kv. and 0.5 mm. Cu filtration (h.v.l. of 1 mm. Cu) was used for the irradiation after 3 mg. of cortisone has been administered subcutaneously in the thigh nine and three hours before the roentgen exposure. One control group of mice was given irradiation only and the second control group was given cortisone only; all the mice of these two groups were alive and well two months later. Of the group (13 mice) receiving both the cortisone and irradiation, 9 died by the eleventh day and the remaining 4 gradually returned to health by the end of two months.

An attempt to study the possible protective effects of glutathione and cysteine proved inconclusive and will be repeated.

A lethal synergistic effect of ionizing irradiation and cortisone is definitely demonstrated. The inhibition of sulfhydryl obligate intracellular enzyme systems by inactivation of the sylfhydryl radical is suggested as a common basic mechanism.—*Dean Nichols, M.D.*

LANGENDORFF, H., SPIEGLER, G., and WACHSMANN, F. Strahlenschutzüberwachung mit Filmen. (Survey of radiation protection with films.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Aug., 1952, 77, 143–153.

1. *Influence of radiation quality upon film blackening and consideration of the hardness factor in dosimetry*. All known films possess a sensitivity markedly dependent upon radiation quality, and the quality of the incident radiation must be known for the use of the "hardness factor" of Dorneich and Schaefer, *i.e.*, the ratio of the amount of incident radiation to that producing optimal density (about 80 kvp.) needed to give the same blackness. The filter method is the simplest way to measure quality; therefore, bakelite film holders with 0, 1.5 mm. Al, 1.5 mm. Cu, and 0.5 mm. Pb filters, covering the front and back of the same quadrant of film, were used. Incidentally, a finger ring with a built-in film holder and filter is shown. Densitometric measurements of the various quadrants, in conjunction with graphs for one special type of German film, lead to an evaluation of the hardness factor, and approximation of the equivalent kvp. of the incident radiation and to determination of the actual dosage.

2. *Further factors to be considered.* (*a*) *Influence of*

exposure time. Unlike the results with visible light, where the density is a function of intensity multiplied by an exponential function of time (exponent 0.85 to 0.95), with roentgen rays the exponent becomes 1, so that there is no loss of blackening because of a prolonged exposure time. (*b*) *Fading of the latent image.* More marked with roentgen rays than with visible light, markedly dependent upon the specific emulsion used, and increasing with increasing temperature and humidity, under normal conditions —room temperature and dry—it may amount to 25 per cent in 45 days. Not a negligible factor, but not unendurable. (*c*) *Influence of angle of incidence.* At 45° density is decreased by 5 per cent, and with a tangential ray by 20 per cent. For practical purposes this can be neglected. The effect of the increase in the path through the filters will increase the "hardness factor" under 80 kvp. and decrease it for higher kvp. (*d*) *Influence of temperature.* The blackening of this film is dependent upon the temperature at the time of exposure. At 60° C. the blackening is only 10 per cent greater than at 20° C., so that under working conditions of room temperature to body temperature, this factor would amount to only a few per cent and can be neglected.

3. *Choice of film.* Sensitivity desired is dependent upon period of observation, a week in England and the United States, and a month in Germany, permitting evaluation of doses of 0.3 to 15 r. A relatively flat density-exposure relationship is advantageous. The less the variation in density with hard and soft radiation, the better. Regression of the latent image should be small. Sensitivity of the emulsion should be constant.

4. *Development and measurement of the film.* A second film with a standard exposure should be developed at the same time to eliminate variables in film sensitivity and development.

5. *Accuracy and comparison with other methods.* If the composition of the incident radiation is known, the accuracy of the method is within 5 or 10 per cent. As used in protection surveys, errors arise, mostly negative, so that about 25 per cent should be added to the estimated dose. Even with exposure to radiation from therapy and radium, the errors are only about 20 per cent. Such errors are permissible. Inherent inaccuracies as compared with ionization chamber or counting tube measurements are offset by integration of prolonged period of time, and absolute certainty of exposure as shown on developed film. The central control of the personnel is simpler, and the sharpness of the images on the film makes it obvious whether the exposure was due to stray radiation, or to getting actually in the direct beam.

6. *Results* In a group of 350 individuals, 79 per cent received 0 to 0.1 r per week, 16 per cent 0.1 to 0.5 r per week, 3 per cent 0.5 to 1.5 r per week and 2 per cent over 1.5 r per week.

7. *Organization.* A central agency for evaluating exposed films is considered better than evaluating them at individual institutions.—*John J. B. Light, M.D.*

Bücker, J. Erfahrungen mit der Hartstrahltechnik und der Feinfokusröhre. (Experience with high kilovoltage technique and the fine-focus tube.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Aug., 1952, *77*, 153–165.

Films with high contrast show good differentiation in the middle density zone, and, with decreased illumination, in the zone of densities below 0.5, but not in the region of densities of 2 and over, even with increased illumination. With 125 kv. (peak) technique, all parts of the structure are in the middle density range, calcific densities not being distinguishable as such in the lung fields from similarly shaped soft tissue densities. The diminution in contrast is partially offset by a decrease in motion unsharpness because of the shorter exposure time, and with the use of the 0.3 mm. focal spot, by decreased geometric unsharpness.

With organs filled with contrast material, such as the stomach, good results are obtained if the secondary radiation is kept low by keeping the irradiated volume small by compression and the use of a small cone, or reduced by the use of a grid or diaphragm. An 8:1 grid ratio yields good results, but a 16:1 ratio is better. Better contrast was obtained at 135 kv. (peak) with a 16:1 grid than at 80 kv. (peak) with an 8:1 grid.

One disadvantage of the fine-focus tube is the lengthened exposure time made necessary by decreased heat capacity, *e.g.*, mucosal relief studies of the stomach done at 0.02 to 0.06 second with a 1 mm. focal spot, needed 0.08 to 0.16 second with the 0.3 mm. focal spot, both being done at 125 kv. (peak).

Numerous illustrations depict exquisite mucosal detail, and make it obvious that, in the average patient, no grid or diaphragm is necessary in fields up to 8 cm. in size.—*John J. B. Light, M.D.*

Pellissier, G. E., and Wicker, E. E. X-ray tin coating gage. *Cathode Press*, 1952, *9*, No. 4, 6–9.

This article, reprinted from *Electrical Manufacturing*, May, 1952, describes in detail the equipment and process used in measuring simultaneously the thickness of tin plating on both sides of sheet iron.

Briefly, a roentgen-ray beam of sufficient energy (12 kv. or more) to excite the K-series roentgen-rays of iron, but not enough to excite the tin K-series (30 kv. or more) is directed upon the specimen, and the secondary emission of fluorescence at the iron-tin boundary is measured at an acute angle by a Geiger tube, the absorption by the tin coating reducing the intensity in proportion to the thickness of the coating.—*John J. B. Light. M.D.*

COUTTS, WALDEMAR E., and SILVA-INZUNZA, EDNA. Contribución al diagnóstico rápido de células cancerosas bajo campo obscuro; communicación preliminar. (Rapid diagnosis of cancer cells by the dark field method; preliminary communication.) *Rev. chilena de hig. y med. prev.*, 1952, *14*, 119–129.

A rapid method of cytodiagnosis is described for cells of urine or other fluid sediments or of tumor scrapings. The material is mixed on the slide with 10 per cent solution of formal and examined microscopically against a dark field. The characteristics of the cancer cells differ considerably from those of the normal cells.

The entire procedure takes only a few minutes.—*L. Guzmán, M.D.*

FALKNER, FRANK, and WISDOM, SYLVIA. Measurement of tissue components radiologically. *Brit. M. J.*, Dec. 6, 1952, *2*, 1240–1241.

In carrying out a detailed growth study on children it is important to know the rates of growth of different tissues. These are mainly bone, muscle, and subcutaneous fat. The authors describe a unique method of measuring tissue components roentgenologically.

Two exposures are made simultaneously on the same film in a plane parallel to the film by two roentgen tubes fixed a known distance apart. Under these conditions the picture shift is a function of the distance of the object from the film. By selecting arbitrary values of this distance, a graph may be obtained giving the distance of an object from the film for any measured picture shift. When the distance of the object is known its actual size may be calculated by measuring the size of the picture of the object on the film, and applying the simple formula $x = x'(K-d)/K$, where x = the true size of the object, x' = its picture size on the film, K = constant distance of the roentgen tube plane from the film plane, and d = distance of the object from the film as calculated above.

This method has been tested with rigid metal objects of a known size and the lower limbs of cadavers and found to be exceedingly accurate.—*William C. MacCarty, Jr., M.D.*

PONSETI, IGNACIO V., and BAIRD, WILLIAM A. Scoliosis and dissecting aneurysm of the aorta in rats fed with Lathyrus odoratus seeds. *Am. J. Path.*, Nov.–Dec., 1952, *28*, 1059–1077.

Epidemic lathyrism has been known to exist for many years in countries where famines have forced the populace to consume a high percentage of legumes in their diet. It affects humans and other animals, producing weakness and spasticity of the lower extremities with urinary and fecal incontinence.

Legumes are deficient in certain essential amino acids, particularly methionine.

For the past three years metabolic studies of a large group of children with idiopathic scoliosis have been carried out at the University of Iowa, and it has been found that the protein metabolism was at fault in these children. There were many points of similarity between the roentgenological characteristics of scoliosis in rats with lathyrism and human idiopathic scoliosis.

Sixteen four week old white male rats were used in the experiments and divided into three groups. Group I consisted of 8 rats and was given a diet of pea meal (ground *Lathyrus odoratus*), cornstarch, sucrose, salt mixture, corn oil, dried yeast and halibut liver oil, plain. Group II, consisting of 4 rats, was fed the above diet with the addition of 10 per cent casein. Group III, consisting of 4 rats, was fed as Group II with the addition of 0.75 per cent methionine. The animals were sacrificed with ether at intervals after the development of scoliosis. Necropsies were performed on all animals.

Roentgenograms taken after two or three weeks of the pea meal diet revealed generalized demineralization of the skeleton. Shortly thereafter periosteal new bone formation appeared, particularly at the level of the femoral metaphysis. Progressive bowing and deformity of the long bones followed the osteoporosis. During the fourth to sixth week of the diet, narrowing and irregularity of the contour of the intervertebral spaces became apparent at the thoracolumbar junction. This was shortly followed by slight forward slipping of the cephalad vertebra over the caudal vertebra at the level of the intervertebral changes. A week later, there was collapse of two to three vertebral bodies at this level with resultant scoliosis. Lateral slipping and vertebral rotation occurred in from one to two weeks and a thoracolumbar kyphoscoliosis was then well established.

Similar changes occurred in the mid-thoracic area two to three weeks later, resulting in the formation of a thoracic kyphoscoliosis. Costal deformities accompanied the rotation of the thoracic vertebrae.

The addition of casein, and of caseine and methionine to the pea meal diet resulted in more rapid growth. This addition of the two substances in no way altered the development of the kyphoscoliosis and its appearance at a younger age is probably due to more rapid growth. This finding substantiates the presence of a toxic factor in the pea meal.

Clinically, the animals were very unhealthy and did poorly. The kyphoscoliosis and rib cage deformities were obvious. Two rats developed paraplegia about ten days before death with dragging of the hind quarters and incontinence. The animals resumed a healthy appearance when placed on a normal diet and although the kyphoscoliosis persisted, they became fat, sleek and active.

The authors conclude that white rats fed a diet containing 50 per cent *Lathyrus odoratus* seeds all

developed kyphoscoliosis. Scoliosis appeared to result from osteoporosis and collapse of several vertebrae. Paraplegia developed in 2 rats with very severe kyphoscoliosis and cord compression.

Aneurysms of the thoracic aorta were seen in 6 of the 8 animals which died intercurrently. The aneurysms developed when the vertebral deformity was still mild.

No toxic lesions were demonstrable in the liver, kidney or other organs.

Lathyrus odoratus seeds appear to contain a toxic factor which affects the formation of organic bone matrix, the aorta and possibly other mesodermal structures.—*C. Peter Truog, M.D.*

Burstone, M. S. A histochemical study of irradiated bone. *Am. J. Path.*, Nov.–Dec., 1952, *28*, 1133–1141.

In an attempt to elucidate the pathogenesis of radiation changes as suggested by earlier work, certain histochemical methods were employed in order to study the bone matrix and related intracellular precursors.

Ten C57 mice, one to three days old, were injected subcutaneously with a carrier-free solution containing radioactive phosphorus, P^{32}, as sodium phosphate. Controls consisted of uninjected immature mice of the same age as well as mice injected with non-radioactive phosphate solution. Another series of 8 three day old mice were injected adjacent to the knee joint with a suspension of chromic phosphate containing P^{32}. The opposite knee joint was also studied as a control. Other controls for this series were injected in the same area with a non-radioactive suspension of chromic phosphate.

Seven days following injection all experimental and control mice were sacrificed. In the control mice, the epiphyseal cartilage and adjacent bones of animals injected with non-radioactive solutions and suspensions appeared histologically identical to untreated controls in all staining reactions.

Changes in the tissues following the local knee-joint irradiation by injection of chromic phosphate and the changes following the local injection of soluble P^{32} solution were practically identical.

From their findings the authors conclude that reactive phosphorus, when administered systemically, or in a local site adjacent to bone, produces a continuous irradiation of the bone marrow. There is a destruction of normal marrow and replacement by abnormal connective tissue cells. These abnormal reticular cells contain greater than normal amount of glycoprotein, glycogen, and alkaline phosphatase, and are associated with a glycoprotein-containing matrix which calcifies.—*C. Peter Truog, M.D.*

Ellinger, Friedrich. Studies on irradiated animals, III. Effect of saline on radiation-induced mortality and weight changes. *Proc. Soc. Exper. Biol. & Med.*, 1952, *81*, 486–489.

Since the "acute radiation syndrome" includes disturbance of salt water metabolism, the author theorized that saline injections might influence the mortality rate following lethal doses of roentgen radiation. This matter assumes great importance in animal experiments, since saline is so frequently employed as a vehicle or solvent for the administration of test substances, or as a control injection.

Mice were subjected to single roentgen-ray doses known to be $LD_{60}/14$ days and $LD_{30}/14$ days. Doses of 0.3 cc. of 0.9 per cent sodium chloride solution were injected either intramuscularly or intraperitoneally, starting immediately after irradiation. Some groups were carried for six days on supportive saline, other groups for fourteen days.

When compared with controls, there appeared to be a statistically significant protection demonstrated in the groups, which received six days of saline injection. However, paradoxically, the death rate rose in those groups receiving fourteen days of saline injection. Gain-in-weight curves run parallel courses.—*Stanley M. Rogoff, M.D.*

Zieler, E. Eigenstrahlung von Kupferfiltern für Röntgentherapie. (Secondary radiation from copper filters in roentgen therapy.) *Strahlentherapie*, 1952, *89*, 288–291.

On the basis of physical measurements, the author concludes that for practical roentgen therapy (with focal-skin distances of 30 cm. or more and with treatment cones with ends closed by plastic materials) an aluminum filter on the patient's side of the copper filter accomplishes nothing worth while. The therapeutically ineffective, but potentially skin-damaging secondary radiation from the copper filter increases the primary radiation approximately 1 per cent if the 1 mm. aluminum filter is removed, whereas insertion of the 1 mm. aluminum filter reduces the total radiation approximately 6 per cent.—*Henry G. Moehring, M.D.*

Moos, Walter S., and Webster, Edward W. An automatic tissue dose computer for use in supervoltage rotational therapy. *Radiology*, Nov., 1952, *59*, 729–736.

In supervoltage rotational therapy, the patient is revolved about a fixed axis, usually the central axis of the tumor which is being irradiated. Therefore, any point, *P*, lying in the plane which passes through the central ray of the beam and perpendicular to the central axis of rotation, will receive a varying dose as it makes a complete revolution about the central axis. The dosage at *P* depends mainly on the distance of *P* from the target of the roentgen tube and the amount of overlying tissue. With 2 mev. roentgen rays backscatter is unimportant.

The authors describe a computer which automatically computes the dosage at point *P* as it ro-

tates about the central axis. For the physical principles upon which the computer is based along with the details of construction and operation, the reader is referred to the original article.

The accuracy of the instrument is considered adequate for clinical purposes. For voltages below 1 mev., corrections for backscatter must be made. The most important limitation of the computer at this time is its inability to take account of the differential densities encountered when irradiating through lung and bone tissue.—*McClure Wilson, M.D.*

CORNEY, G. M. Relation of film characteristics to x- and gamma-ray monitoring. *Nucleonics*, Nov., 1952, *10*, 84–86.

Calibration of films requires a knowledge of radiation quality to which they have been exposed. In medical diagnostic roentgenography the quality is essentially similar to the primary radiation, and in the voltage range used the film sensitivity does not vary more than 10 per cent. In calibrating films, any voltage in the range may be satisfactorily used.

In industrial roentgenography, calibration with as heavy filtration as possible for practical purposes should be used, so that the monitoring films will properly evaluate radiation through protective barriers, and overvalue the scattered radiation, the resulting error leading to increased safety.

Filters do not compensate entirely for wavelength dependence, and the limitations of a particular filtration technique must be understood before it is applied. The best that can be done is to choose filter thicknesses such that, when filter-film combinations are calibrated with normally incident radiation, the radiations incident at other angles are overvalued rather than undervalued.

Graphs of relationship of kv. (peak) to r necessary to produce a film of density 1.0, and of variations in density with varying development times for same exposure, and with variations in temperature and exhaustion of developer are given.

It is pointed out that, over a limited range, there is a linear relationship between density and exposure for non-screen film.—*John J. B. Light, M.D.*

CASTRO, PEDRO L. La radiografía de acecho. (Spot film roentgenography.) *Arch. Hosp. Universitario*, Habana, July–Aug., 1952, *4*, 393–435.

Spot film roentgenography has been used for years but due to the great technical improvement in the design of apparatus its range of applicability has recently been considerably widened.

The author, in the present article, gives numerous examples selected from his private practice of the last six months in which the method has proved particularly valuable and he includes beautiful reproductions of the respective spot films to illustrate the pertinent points.

Respiratory Apparatus. In conjunction with this apparatus the use of spot films is of greatest value in bronchography. The author instills the iodized oil under fluoroscopic control and immediately after the site of the alteration is localized makes spot film exposures in the desired views, thereby often shortening the time of examination considerably.

Digestive Apparatus. As is known, the gastrointestinal tract with its different sections of varying physiologic motions lends itself most admirably to extensive use of spot film roentgenography. The author passes in review the following possibilities: study of the passage of the barium meal through the esophagus and differentiation of organic lesions from spastic contractions; serial study of the lower end of the esophagus; differential diagnosis of gastric ulcer and neoplasms; study of the deformity of the duodenal bulb where the method is absolutely indispensable; demonstration of duodenal fistulas; determination of the site, appearance, tenderness and movability of the appendix in chronic appendicitis; study of the filling of the biliary tree in postoperative cholangiography; clearer visualization of the gallbladder shadow in the prone decubitus, and when using the Åkerlund or Kirklin techniques; relief study of the terminal ileum; simple and double contrast study of the colon and exploration of the rectosigmoid junction.

Nervous System. Spot films are used advantageously in myelography by tilting the table to various degrees and making the exposure when the opaque column passes through the suspected area of alteration.

Urinary Apparatus. In the roentgen examination of this apparatus the author favors spot film exposures for the demonstration of small filling defects of the kidney pelvis, papillae and calyces, and especially for the study of pyelectasias in visualizing small retentions of the opaque medium which may be indicative of an organic lesion.

Female Genital Apparatus. Hysterosalpingoscopy associated with spot film exposures is, according to the author, superior to any other roentgenologic method of examination in gynecology since it permits visual control of the injection of the opaque medium. Thus, an accidental injection of the venous and lymphatic plexuses or the passage of too much oil into the peritoneal cavity, leading later to the formation of oleomas, can be avoided. Furthermore, the time of the examination is markedly shortened.

The general conclusion is reached that spot film roentgenography helps considerably in improving the accuracy of the diagnosis, especially in those tracts or organs in which the changing physiologic movements necessitate precise recording of the findings in various phases of the movement.—*T. Leucutia, M.D.*

BELL, A. L. L., MAGOVERN, JOHN J., and

Zwanger, Jerome. A simple immobilization apparatus for radiography of the newborn. *Radiology*, Feb., 1953, *60*, 265–266.

A simple, easily constructed device for immobilization of infants during roentgenography is described and illustrated by a photograph. Its value has been proved by consistently good roentgenograms. A substantial reduction in radiation exposure to patient and personnel is claimed.—*Arno W. Sommer, M.D.*

McClure, Richard F., Doub, Howard P., and Shipley, Richard E. Automatic cassette changer for angiography. *Radiology*, Jan., 1953, *60*, 85–89.

The authors describe an automatic cassette changer for angiography which they have developed. This apparatus is a modification of that of Campbell and Lockhart and was devised in an attempt to overcome the difficulties attendant upon hand operation.

The machine is driven by an electric motor. Freedom from jamming has been accomplished by passing all moving parts over roller bearings.

The present model of this device permits the exposure of films at rates of one per second or two per second. Either speed can be accomplished by adjusting the position of the V-belt between two step-V pulleys.

The roentgen equipment used with this device is a 200 ma. rotating anode tube with a timer permitting exposures from 1/20 second.

The cost of construction should be about $500.00.

Interested readers should refer to the original article for mechanical construction and operation.—*Arthur Watson, M.D.*

Crooke, A. C. Endocrine glands and growth. *Schweiz. med. Wchnschr.*, Feb. 21, 1953, *83*, 194–198.

Growth may be defined as the anabolism of new protoplasmic tissue in excess of catabolism. It affects all tissues and is influenced by many different factors. Under favorable circumstances, the growth of an animal follows a uniform pattern. When the weight as a percentage of adult weight is plotted against age from birth to adulthood, it is found that the curves obtained are very similar for a wide variety of species. The growth curve of man, however, differs from those of other species and can only be fitted to the common curve during the adolescent growth period. These differences are undoubtedly genetically determined, but it is of interest to investigate whether they are influenced by different hormonal factors as well. For this purpose, it is proposed to compare the primary endocrine factors concerned with the skeletal growth of the rat and of man, the rat being chosen as a typical representative of the usual growth curve of lower animals.

Two components in skeletal growth must be considered, one of which is measured by increase in size, and particularly in length, of the axial and appendicular skeleton, and the other by differentiation of the ossification centers and their subsequent maturation and fusion.

From ablation and hormonal replacement experiments, it is evident that in the rat growth in length is primarily under the control of the pituitary growth hormone, whereas the development of ossification centers and maturation are primarily under the influence of thyroxin. There is little to suggest that any of the other hormones play a predominant part in either process.

It is obviously more difficult to obtain a precise assessment of hormonal factors influencing growth in man. However, by comparison of the endocrinopathies with animal experimentation, it is possible to make an estimate of the alteration in hormonal balance produced, and to obtain an insight into the reason why the relative growth rate of man differs so remarkably from that of most other animals.

Dwarfism due to destructive lesions of the pituitary gland is associated with the loss of pituitary function involving the trophic hormones to a variable extent. There is an arrest or slowing of growth in length and of bony maturation, with clinical evidence of deficiency of thyroid, adrenocortical and gonadal secretions. A close parallel may be drawn with hypophysectomized rats, and it may be assumed that failure of growth in length is due to a deficiency of growth hormone and failure of bony maturation to a deficiency of thyroid and perhaps gonadal secretions. However, the pituitary dwarf differs from the hypophysectomized rat by being relatively insensitive to treatment with growth hormone. Also, bony maturation does not occur when dwarfs are treated with thyroxin. Instead, they respond by growth of both types when treated with gonadotrophic hormone or testosterone.

In cretins, growth in length and in skeletal maturation are again severely retarded. These respond rapidly to treatment with thyroxin, but not to growth hormone, presumably again because of the relative insensitivity of man to this substance. In other respects, they are comparable to thyroidectomized animals.

Castration before puberty has a far more profound effect upon the skeleton of man than of the rat, and it seems likely that androgens exert a stronger stimulus both to growth in length and to bony maturation in man than in most animals. Estrogens exert a very similar skeletal effect, and it has been suggested that women have a shorter stature because of the earlier onset of puberty and the consequent earlier influence of estrogens on the closing of epiphyses.

Patients with ovarian agenesis have a dwarfed stature, but only moderate delay of bony maturation. In these cases, the sex hormone production possibly is insufficient to cause the normal growth spurt at puberty, but sufficient to cause epiphyseal fusion

before the normal adult stature is achieved.

Probably all giants are the result of an excessive secretion of pituitary growth hormone and the larger the giant, the earlier in life the disease began. Growth continues steadily with no obvious pubertal exacerbation until the maximal height is reached. Frequently, there is an associated deficiency of gonadotrophic hormone with resultant failure of pubertal development and of bony maturation. Thus, while at first glance these giants may appear to be suffering from excessive growth hormone alone, later they may bear a superficial resemblance to the hypophysectomized rat treated with excessive growth hormone; that is, there is an excessive growth, but bony maturation is delayed as a result mainly of gonadal failure in man and thyroid failure in the rat.

Thyrotoxicosis in childhood has a definite tendency to stimulate growth in length and early bony maturation. There is no question that thyroxin affects bony maturation in man in the same way that it does in the rat, but it is not the only major endocrine factor in man. Moreover, it may have a greater effect in stimulating growth in length than in the rat.

Precocious puberty occurs as a result of an interesting variety of pathological disorders. In one group of cases, certain hypothalamic lesions may be the causative factors. The gonadotrophic and steroid hormone output in these children is of the order of that found in adults. Consequently, they grow abnormally fast, but epiphyseal fusion is premature so that their final adult height is less than normal.

Another group of cases of precocious puberty results from secreting tumors of the testes or ovaries. In these, the steroid secretion from the gonads may be at a very high level while gonadotrophic secretion is low.

The third group results from secreting tumors or hyperplasia of the adrenal cortex, in which cases the steroid secreted is nearly always androgenic. In both these latter groups, the skeletal changes are similar to those found in the hypothalamic group. They give the clearest evidence available of the profound effect of the sex steroids in stimulating growth and bony maturation in man.

In Cushing's syndrome, there is an excessive production of cortisone-like 11-hydroxycorticoids and growth appears to be inhibited. A parallel of this is seen in cortisone treated rats from which it appears that these substances oppose the action of the growth hormone.

Thus, a study of the influence of the various endocrine diseases on growth may help explain why the growth curve of man differs from that of various lower animals.—*William C. MacCarty, Jr., M.D.*

RICHARDS, ALBERT G. Selective control of roentgenographic contrast with radiopaque media. *J. Am. Dent. A.*, Feb., 1953, *46*, 187–196.

The author describes detailed and painstaking roentgenographic studies on extracted teeth for the purpose of improved visualization of tooth structure.

Considering that a roentgenogram is a record of shadows produced by the differential absorption of the beam of roentgen rays by the tissues and structures it traverses, the author substituted radiopaque media of varying density for the air surrounding the tooth. This results in improved dentine-enamel contrast, decreased fogging from secondary radiation and the demonstration of clear and adequate detail within the tooth.

Roentgenographic contrast is affected by tube voltage, tooth-film distance, depth and density of the radiopaque medium surrounding the tooth.

The usefulness of the method is limited to studies of extracted teeth for research and teaching purposes and is not applicable to the mouth of a living patient.

Numerous illustrations, tables and charts accompany the article.—*William H. Shehadi, M.D.*

ESSENBERG, J. M. Cigarette smoke and the incidence of primary neoplasm of the lung in the albino mouse. *Science*, Nov. 21, 1952, *116*, 561–562.

The author devised a machine which subjected experimental mice which were known to be susceptible to lung tumors to cigarette smoke for periods of about one year.

After careful microscopic examination of the lungs of the experimental animals and of an equally large control group, it was found that tumors of the former group exceeded those in the control series by 31.9 per cent. There was no difference in the two groups except the exposure to smoke for a period of about one year. It was also noted that the experimental group of animals failed to reproduce normally and that their weight and growth curves were lower than those of the control group.

The author therefore concludes that some factor or factors in the cigarette smoke was carcinogenic in this particular experiment.—*Lawrence A. Davis, M.D.*

WEIGEN, JOHN F., PENDERGRASS, EUGENE P., RAVDIN, ISADORE S., and MACHELLA, THOMAS E. A roentgen study of the effect of exclusion of pancreatic juice from the intestine on gastrointestinal motor activity in the dog. *Radiology*, Feb. 1953, *60*, 252–256.

This paper is a follow-up on a previous one by the same authors in which they demonstrated that hyperglycemia in depancreatized dogs was associated with a marked delay in gastrointestinal motility, while in insulin-induced hypoglycemic animals, normal, and at times rapid gastric emptying and small intestinal transit times were noted.

The experiments described in this paper were to determine what influence if any the external pancreatic secretions had on gastrointestinal motility.

The gastrointestinal tracts of these dogs were examined roentgenographically, and then again one week later following ligation of the pancreatic ducts. Special attention was paid to gastric emptying time, tone and motility and to small intestinal transit time, tone and continuity of pattern.

The authors conclude that exclusion of external pancreatic secretion from the intestine of the dog appeared to cause no alteration in motility or tone of the gastrointestinal tract. The delayed gastrointestinal motility in depancreatized dogs during hyperglycemia must be considered as being due to the elevated blood sugar and not to the loss of external secretion of the pancreas.—*Donald N. Dysart, M.D.*

Haley, Thomas J., and Rhodes, Bonnie M. Influence of peripheral cholinergic blocking drugs on survival time in x-ray irradiated mice. *Science*, Feb. 6, 1953, *117*, 139–140.

There is a difference of opinion regarding the role played by the cholinergic branch of the autonomic nervous system in the radiation syndrome.

Some workers (Burnett, Burke, Upton) have shown that cogeners of acetylcholine protected C_{57} strain mice from lethal effect of roentgen radiation while atropine could counter such a protective action. Larkin, however, found that atropine increased the survival time in CFI roentgen irradiated mice.

Male CFI strain mice, average weight 20 grams each, were placed in groups of 20 animals.

Beginning one day prior to irradiation and until 90 to 100 per cent of the animals died (10 to 16 days) each animal received a daily intramuscular injection of 0.1 ml. of the following concentrations of peripheral cholinergic blocking drugs: Group I, 0.45×10^{-3} M; Group II, 0.90×10^{-3} M; Group III, 1.35×10^{-3} M, while the controls received 0.9 per cent saline solution.

The drugs used were atropine; Merck MK-02 (tropine benzohydryl ether methanesulfonate); Win-2299 (1-methyl-3-piperidyl-methyl-phenyl-2-thenyl-acetate); and Bentyl (1-cyclohexylhexahydrobenzoic acid, β-diethylaminoethyl ester). A dose of 550 r was administered from above and below, simultaneously by two 250 kv (peak) Picker Industrial units over the entire body at a rate of 17.2—18.4 r/min.

From the results obtained it is evident that none of the drugs had a significant effect on total mortality and that such medication cannot be considered highly beneficial in counteracting overall radiation injury.—*William H. Shehadi, M.D.*

Watson, J. S., Jr., Weinberg, Sydney, and Ramsey, G. H. A 70-mm. cinefluorographic camera and its relation to detail. *Radiology*, Dec., 1952, *59*, 858–865.

The cinefluorographic record is a valuable aid in clearing up doubtful fluoroscopic findings having to do with disturbances of swallowing, calcification within and around the heart, and abnormal movements of the diaphragm or mediastinum. When cinefluorography is applied to subjects outside the fluoroscopic range the lack of definition becomes an undesirable factor.

Methods which may be used to improve cinefluorographic detail are discussed. The authors' studies were made with a new camera having a picture aperture measuring 53 by 37 mm. as compared with the 18 by 24 mm. frame of the standard camera. Experimental determinations were made of 35 mm. and 70 mm. detail at three stages of magnification with the old resolving power or "lines per millimeter" method. Tests indicated that 70 mm. detail is superior to 35 mm. detail. The 70 mm. negative is also easier to study, frame by frame, than the 35 mm. negative.

Detailed description of the new camera is given and photographs of the equipment are included.—*Arno W. Sommer, M.D.*

Gilardoni, Arturo, and Schwarz, Gerhart S. Magnification of radiographic images in clinical roentgenology and its present-day limit. *Radiology*, Dec., 1952, *59*, 866–878.

An enlarged roentgenographic image may be desired (a) for greater facility in demonstration of lesions to audiences; (b) for extending the range of information available from a film.

Two principal methods of image magnification are now practical: (a) Roentgenographic, employing a 0.3 mm. focal spot tube. The inherent limit of magnification is a useful linear enlargement of $\times 2$. This method is at present limited to parts of the body which can be completely immobilized, due to the long exposure times required.

(b) Photographic, giving a possible enlargement of $\times 2$ of roentgenograms of almost all body parts, taken with conventional equipment. The roentgen tube must have a focal spot of no greater than 2 mm. effective size, and high definition screens or a no-screen technique must be used. Modifications of conventional photographic techniques are used for the enlargement. With optional conditions, maximal useful linear photographic enlargements of about $\times 10$ can be produced.

With development of other types of films, or more powerful fine focus tubes, higher magnifications will be possible.—*L. J. Taylor, M.D.*

Gilardoni, Arturo. Ingrandimento dell'immagine roentgen con metodo radiologico ed ottico. (Enlargement of the roentgen image by roentgenologic and optic methods.) *Radiol. med.*, Jan., 1953, *39*, 48–57.

The author at the First Radiologic Congress of Latin Culture held in Brussels, Belgium, in July, 1950, presented the results of his investigations on

the enlargement of the roentgen image by means of the roentgenologic and optic methods. Recently he continued these investigations in the United States in collaboration with Dr. Schwarz of the Presbyterian Hospital, New York, and also studied the possibility of combining the two methods.

In the present article he gives a detailed account of the various problems encountered and of the procedures pursued in trying to solve them.

The following general conclusions are reached:

(1) The presently employed roentgenologic method using focal spots of 0.3 by 0.3 mm. with an increased object-film distance permits a maximum linear enlargement of two times (or four times of the surface). This limitation is an inherent characteristic of the method. The capacity of tubes with such small foci, even when rotating anodes are provided, is too small to permit good roentgenograms of dense or mobile parts of the body. The procedure furthermore requires expensive vibration-free tube stands and specially devised accessories for immobilization of the patient.

(2) The optic photographic method permits a useful enlargement of two times of practically all parts of the human body using a normal tube with a 2 by 2 mm. focal spot and fine grain screens. Thin parts, as for example the hand, can be linearly enlarged to ten times (or one hundred times of the surface) without the use of screens. For linear enlargement up to two times, an ordinary lens 100 mm. in diameter with an enlarging factor of two is sufficient; for greater enlargement in the presence of a good negative an ordinary photographic magnifier may be employed.

(3) In practice, a linear enlargement to twice the size does not enhance significantly the diagnostic possibilities.

(4) The useful enlargement cannot be increased further by combining the two methods since the upper limit of permissible fogginess has already been reached in the magnified image obtained by the roentgenologic method in its present form.—*T. Leucutia, M.D.*

AMORY, HAROLD I., and SMITH, SCOTT W. Military field x-ray equipment. *Radiology*, Dec., 1952, *59*, 879–892.

This is a progress report to inform the medical profession of the present status of military field roentgen-ray equipment and of the current concept of military roentgenology. General and specific problems of military roentgenology are discussed. Equipment designed to meet the needs of radiologists in mobile surgical hospitals is described and illustrated. Although the equipment varies considerably in many respects from commercial units, nothing considered essential for high quality roentgenography and fluoroscopy has been sacrificed.—*Arno W. Sommer, M.D.*

INLOW, HERBERT H. Modification of the Bardex-Weber enema tube. *Radiology*, Feb., 1953, *60*, 267.

By placing a solid rubber ball about $\frac{1}{8}$ inch proximal to the bag of a Bardex-Weber enema tip, the author avoids leakage of barium around the inflated bag. A hole is drilled in the $2\frac{3}{16}$ inch diameter ball which is then slipped over the proximal tube with the aid of a pair of forceps and then cemented in place.—*Martin B. Goodwin, M.D.*

GEIST, ROBERT M., JR., GLASSER, OTTO, and HUGHES, C. ROBERT. Radiation exposure survey of personnel at the Cleveland Clinic Foundation. *Radiology*, Feb., 1953, *60*, 186–191.

A three month survey of all workers associated in any way with radiologic procedure was conducted at the Cleveland Clinic to determine the dose of radiation received per week.

Film badges with various filters and containing special film were used. The film was developed and the exposure to milliroentgens determined by Tracerlab, Inc.

A detailed description of the project is given.

The tolerance dose of 300 mr per week was exceeded only when a technician immobilized too many patients manually and occasionally in the case of the operators of the radon plant. The radon plant has since been dismantled and immobilization devices have been constructed.

Of the special procedures, angiocardiography, using a rapid cassette changer, showed an average exposure of 92 mr to the team per examination, but only an average of one such examination was done per week. Otherwise, the exposure to personnel throughout the entire diagnostic and therapeutic sections was well below the tolerance dose.—*Martin B. Goodwin, M.D.*

LAUGHLIN, J. S., OVADIA, J., BEATTIE, J. W., HENDERSON, W. J., HARVEY, R. A., and HAAS, L. L. Some physical aspects of electron beam therapy. *Radiology*, Feb., 1953, *60*, 165–185.

Using as an electron source a 22 mev. betatron, the installation and controls of which are described, the authors have extensively investigated, and related to practical therapeutic usage, the physical characteristics of the high energy electron beam which seems most useful for such applications.

A radiation survey was made for roentgen rays and low energy electrons, thermal neutrons, and fast neutrons. Ionization distributions and depth doses were measured in a water-tank phantom, and isodose contours were charted. Specific ionization of electrons in air was recorded.

Dosimetry problems were investigated, and Faraday cage measurements used to express beam intensity in ergs/cm.^{2} and amperes/cm.^{2}. The problems of

integral dose were related to this type of beam.

The above investigations are described as to equipment and methods used, results obtained, and useful formulas evolved.

Among the practical applications of interest are these:

A rather definite maximum depth of penetration exists, which is directly proportional to the incident energy, and is therefore conveniently adjustable. The rate of decrease is steep near the end of the penetration. Both these characteristics become less marked with increasing beam intensity.

Side scatter, being of greater magnitude than in the case of betatron roentgen rays, prevents formulation of equally simple isodose contours.

High intensities are available, rates exceeding 20,000 r/min. having been measured.

Absorption of this type of beam will not vary with the atomic number of the absorbing material as much as will that of low energy roentgen rays.

Such features make this type of beam ideally applicable for the therapy of lesions adjacent to the body surface, since it is possible to expose the lesion rather uniformly from the skin surface to any desired depth, with a rapid decrease of irradiation beyond this depth.—*Lynne J. Taylor, M.D.*

Graham, Ruth M., and Graham, John Barkley. A cellular index of sensitivity to ionizing radiation; the sensitization response. *Cancer*, March, 1953, *6*, 215–223.

The cells of the deep epithelial layer of the vagina and cervix may show changes which might serve as an index of radiation sensitivity. These changes may be observed in both animals and humans.

Previous work by the authors has shown that cell changes in vaginal and cervical mucosa following irradiation may be of prognostic significance. This cytological radiation reaction (RR) was calculated as a percentage of the benign squamous cells showing: vacuolization of the cytoplasm, size increase, double nuclei and nuclear changes. If 75 per cent of the cells showed these changes, the patient was regarded as sensitive to radiation. In a group of 125 patients with primary carcinoma of the cervix so analyzed, 37 (59 per cent) of 63 showing good cytological response lived five years, while only 2 (3 per cent) of the 62 showing poor response lived five years.

Study of pre-irradiation cervical smears showed a similar "radiation" effect in some cases. These patients were subsequently found to be among those sensitive to irradiation.

Work on animals (mice) has shown that vacuolization in vaginal basal cells would follow the injection of steroid hormones. In addition, the cytoplasm changed color from green or pink to a deep lavender. The mice showing this effect were more sensitive to irradiation. This tendency toward increased sensitivity was called sensitization response (SR). This response was interpreted to mean that, if a patient or animal were irradiated at the time these cells are present, that individual would be more sensitive to irradiation than if the cells were not present.

One hundred patients were studied for SR. At least 100 nonmalignant cells were counted in each cervical smear made prior to irradiation. SR was considered significant when 10 per cent or more of the nonmalignant cells showed lavender, vacuolated cytoplasm with red granules.

Among the 100 patients, 35 showed a significant SR; 66 per cent (23) of these are living and well five years. Of the 65 patients showing no significant SR, 82 per cent (53) are dead and only 18 per cent (12) are living and well at five years.

Many photomicrographs accompany the paper.—*I. R. Berger, M.D.*

Deuel, Harry J., Jr., Cheng, Amber L. S., Kryder, George D., and Bingemann, M. E. The protective effect against x-irradiation of methyl lineolate in the rat. *Science*, March 6, 1953, *117*, 254–255.

The Department of Biochemistry and Nutrition at the University of Southern California, Los Angeles previously showed that rats receiving a diet containing a small amount of cottonseed oil were much more resistant to injury from roentgen irradiation than those on a fat free regimen. The difference was noted when sublethal doses were given over a period of time. There was no difference if the rats were subjected to a single lethal dose.

The present experiments were designed to demonstrate whether the effect of cottonseed oil was due to an essential fatty acid such as methyl lineolate. Ten milligrams of methyl lineolate were given to each of a group of rats that were on a basal fat free diet and a control group received none. It was found that the survival time of the rats receiving methyl lineolate was significantly greater from a statistical standpoint than of those which received none. The exposure to roentgen irradiation was also greater in the group receiving methyl lineolate.

It is not definitely known why methyl lineolate has a beneficial effect on irradiation injury. It is believed to be linked to the nutrition of the epidermis as fatty acid deficiency produces an eczematous condition and scaliness of the skin of the tail in the rats. Other substances such as cystine, ascorbic acid and vitamin P have been found to be important in metabolism of the epidermis and are of advantage in irradiation injury.—*Charles W. Cooley, M.D.*

Lisco, Hermann, and Kisieleski, Walter E. The fate and pathologic effects of plutonium metal implanted into rabbits and rats. *Am. J. Path.*, March-April, 1953, *29*, 305–321.

Previous studies of the metabolism of plutonium have been made with salts of the metal in solution. These have shown that the metal is fixed in the liver,

spleen and bone in amounts of 70 to 80 per cent of the injected dose. Very little is excreted over periods of months to years. The present study is concerned with determining the absorption of the metallic form from the subcutaneous tissues of rats and rabbits.

After subcutaneous implantation of plutonium metal, the experimental rats (3) and rabbits (8) were permitted to live out their life span. Excretion studies on the rats showed after fifteen weeks urinary excretion of 0.001 microgram weekly and fecal excretion of 0.044 microgram weekly. This diminished over a period of ten months. In rabbits after two months barely measurable amounts were detected in the urine and none in the feces.

Absorption was determined afetr death (2 to 1,048 days) by measuring the plutonium in selected tissues (liver, spleen, kidneys, lungs, testes and bones). Average absorption was less than 0.5 per cent with a range of from 0.09 to 1.2 per cent. Rabbits absorbed three times as much as rats. There was no correlation between either the amount of plutonium implanted or survival time and absorption. Rabbits concentrated 55 per cent of plutonium absorbed in the liver and 44 per cent in the skeleton, whereas rats concentrated 6 per cent in the liver and 85 per cent in the skeleton.

The sites of implantation showed marked fragmentation of the metal, heavy calcification and demarcating connective tissue. No local skin changes were present. One rat developed an osteogenic sarcoma of the spine after ten months.

In conclusion it is noted that considerable quantities of unmetabolized plutonium may be present in the subcutaneous tissues without showing evidence of this in the excreta.—*Henry J. Klos, M.D.*

GOULD, S. E., VAN DYKE, JAMES G., and GOMBERG, HENRY J. Effect of x-rays on trichina larvae. *Am. J. Path.*, March–April, 1953, *29*, 323–337.

Other experimenters have shown that both roentgen and gamma radiation can effectively attenuate or destroy trichinae by either preventing the larvae from maturing or by rendering sterile any adults that develop. The authors' purpose was to determine the dosages necessary to destroy larvae, to prevent maturation of larvae and to sterilize the trichinae, all in vitro, and then to determine the dosage necessary to control larvae in white rat muscle.

The trichina larvae were irradiated by a 200 kv. unit with either inherent filtration or added 0.5 mm. of copper. Irradiation was completed within minutes to hours, the output of the unit being of the order of 1,000 r per minute.

Using motility of the larvae in warm water as a criterion of viability, it was found that 750,000 r was necessary to render all larvae nonviable within forty-eight hours in vitro. By feeding larvae irradiated in vitro to white rats and then counting the adult forms in the small intestine of the sacrificed animals, a measure of maturation was obtained. These studies showed that between 4,000 and 6,000 r markedly reduced or entirely prevented maturaton to adult forms in the small intestine. A measure of reproduction of any adult forms that developed was obtained by macerating the muscle of the rat, digesting it, then counting the larval forms. It was found that adult trichinae developing from larvae irradiated with over 4,000 r yielded virtually no larvae obtainable from muscle.

Larvae were then irradiated in vivo, in rat muscle, and fed to uninfected rats. Dosages of 12,500 r were necessary to significantly retard maturation of the larvae in the intestine and 15,000 r was necessary to prevent such maturation entirely. Thus, considerably larger doses are necessary in vivo than in vitro.

The authors conclude that exposure to 15,000 r of roentgen radiation is necesssary to render trichina larvae sterile in vivo. This suggests that the irradiation of pork in commercial quantities may not be impractical.—*Henry J. Klos, M.D.*

GECKLER, R. P., and KIMBALL, R. F. Effects of x-rays on micronuclear number in *Paramecium aurelia*. *Science*, Jan. 23, 1953, *117*, 80–81.

The authors report on experimental studies concerning micronuclei following irradiation of *Paramecium aurelia*. They state that there is circumstantial evidence against loss of microneuclei following irradiation but no actual evidence. Accordingly, groups of *Paramecium aurelia* were subjected to doses ranging from 214 to 537 kr and studied after a suitable waiting period and after fixation and dyeing. Only at doses above 400 kr were appreciable numbers with less than two micronuclei produced. Reduced vigor and death were noted at much lower dosages.

The authors conclude that the present study tends to indicate that loss of micronuclei is not a major reason for the reduced viability of *Paramecium aurelia* exposed to roentgen rays.—*P. B. Parsons, M.D.*

v. BRANDT, HILDTRAUT, and HÖHNE, GÜNTER. Mutationsauslösung bei der Taufliege Drosophila melanogaster durch schnelle Elektronen eines 6 MeV-Betatrons. (Induction of mutations in *Drosophila melanogaster* by fast electron beam from a 6 mev. betatron.) *Strahlentherapie*, 1953, *90*, 93–99.

No significant difference exists between a fast electron beam and conventional roentgen or gamma rays in inducing recessive sex-linked lethal mutations via exposure of either mature sperm or immature germ cells of *Drosophila melanogaster*. However, the same doses of radiation produce considerably fewer mutations when applied to immature germ cells than when applied to mature sperm.—*Henry G. Moehring, M.D.*